

PATENT ABSTRACTS OF JAPAN

(11)Publication number : 05-025158

(43)Date of publication of application : 02.02.1993

(51)Int.Cl.

C07D311/04

C07D311/66

C09K 19/42

C09K 19/54

C09K 19/58

G09F 9/35

(21)Application number : 03-273021

(71)Applicant : KANTO CHEM CO INC

(22)Date of filing : 23.07.1991

(72)Inventor : TSUCHIYA KAZUHIKO

SUGIURA ATSUSHI

SUZUKI KENJI

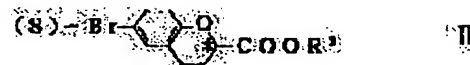
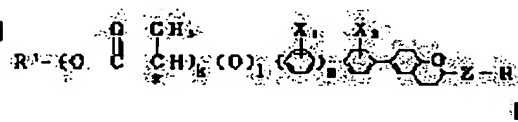
FUJII TSUNENORI

(54) CHROMAN DERIVATIVE AND LIQUID CRYSTAL COMPOSITION CONTAINING THE SAME

(57)Abstract:

PURPOSE: To provide a new compound containing chroman skeleton, having excellent chemical stability and useful as a ferroelectric liquid crystal component.

CONSTITUTION: The compound of formula I (R1 is 1-14C alkyl; R2 is 1-14C alkyl; (k), (l) and (m) are 0 or 1; Z is single bond, CO-O or CO; X1 and X2 are H or F; * represents optically active C), e.g. 2-heptyl-6-(4-decyloxyphenyl)-chroman. The compound of formula I can be produced by the coupling reaction of a compound of formula II with a compound of formula III in the presence of a Pd catalyst. The ferroelectric liquid crystal is useful as a display element for watch, electronic calculator, personal word-processor, pocketable TV, etc.



LEGAL STATUS

[Date of request for examination]

[Date of sending the examiner's decision of rejection]

[Kind of final disposal of application other than the examiner's decision of rejection or application converted registration]

[Date of final disposal for application]

[Patent number]

[Date of registration]

[Number of appeal against examiner's decision
of rejection]

[Date of requesting appeal against examiner's
decision of rejection]

[Date of extinction of right]

Copyright (C); 1998,2003 Japan Patent Office

* NOTICES *

JPO and NCIP are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001] [Technical field] This invention relates to the liquid crystal constituent characterized by containing at least one sort of these liquid crystallinity compounds in a new liquid crystallinity compound list. Furthermore, if it says in detail, about a ferroelectric liquid crystal, in the case of practical ferroelectric liquid crystal constituent production, this invention is useful as the presentation component, and relates to the liquid crystal constituent containing at least one sort of a liquid crystallinity compound which has those new chroman frames in the liquid crystallinity compound list which has the new chroman frame excellent in chemical stability.

[0002] [Background of the Invention] -- the time -- the object for total, calculator, personal word processor, and pocket television etc. -- the liquid crystal display component is widely used as a display device. this is a thin shape with little power consumption to which an eye is not tired with a light-receiving mold -- etc. -- although it was because it has the outstanding description, in an application side, there was a limit from there being no memory nature with a slow speed of response in one side etc. In order to aim at expansion of an application side, the super-twisted-nematic (STN) mold means of displaying which improved the Twisted Nematic (TN) mold means of displaying used conventionally is found out. However, these are not enough as a big screen display or an object for graphical display, and various researches of the liquid crystal display component replaced with these are also done.

[0003] He is ferroelectric liquid crystal [R.B.Meyer et al. to one of them ;P There is means of displaying [N.A.Clark;Applied Phys.lett., 36,899 (1980)] using hysique and 36L-69(1975)].

[0004] Since this method has the outstanding descriptions, like that it is a 1000 times [no less than] as many high-speed response as this and there is memory nature compared with the conventional method, application expansion of a liquid crystal display component is expected. Although a ferroelectric liquid crystal points out the smectic liquid crystal with which a liquid crystal molecule major axis has the direction of a layer normal, and a certain include angle, a chiral smectic C (chiral SmC) phase is used practical especially.

[0005] The ferroelectric liquid crystal for display device production is used as a liquid crystal constituent which mixes the compound and optically active compound which have the SmC phase of the compounds which have various chiral SmC phases, or (1) (2) versatility, and is obtained. Although researches and developments of a ferroelectric liquid crystal display device used the liquid crystal constituent obtained by the method of (1) at the beginning, since it became clear that a ferroelectric liquid crystal was obtained by adding an optically active compound to the compound which has a SmC phase, it has been tended for researches and developments to progress, and to use the constituent obtained by the method of (2).

[0006] The approach of adding - [one sort of] several sorts of optically active compounds (called a chiral dopant with the compound it is not necessary to necessarily have, although it is better to have the chiral SmC phase) to the SmC constituent (SmC host) which mixes especially a SmC compound and is obtained, and producing a ferroelectric liquid crystal constituent is becoming in use.

[0007] Since a SmC compound is cheaply compoundable compared with that this tends to adjust the various properties (an operational temperature range, a speed of response, spontaneous

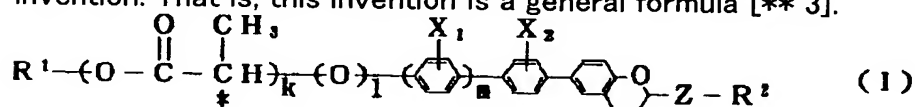
polarization, a RASEN pitch, chemical stability, etc.) that the direction of (2) is required from a commercial scene, in a practical use side, and a chiral SmC compound, it is because (2) is considered to be advantageous. However, development of the compound with which practical use does not yet come to be presented and which can serve as a useful component in the case of ferroelectric liquid crystal constituent production is desired.

[0008] It is raised to one of the properties required of a chiral dopant that the spontaneous polarization of the ferroelectric liquid crystal constituent obtained by adding it to a SmC host is large.

[0009] This will be because the response time can be shortened, if spontaneous polarization is enlarged so that clearly from relational-expression $\tau = \eta / P_s E$ (τ = response time, η = viscosity, E = electric field, P_s = spontaneous polarization) of the response time and spontaneous polarization in a ferroelectric liquid crystal.

[0010] About the relation between spontaneous polarization and the molecular structure of a chiral dopant Although it does not escape from the region of the rule of thumb of a various-views **** thing but there is still no steadfast thing, if the free rotation of a part with the dipole moment in the molecular structure which makes one in them discover "ferroelectricity can be controlled There is an opinion that it can become possible to make the dipole part as the whole go in the fixed direction, and spontaneous polarization can be enlarged" (refer to JP,2-138274,A). Moreover, the compounds (JP,1-250335,A etc.) which introduced the halogen atom in dimension height the large naphthalene derivatives (JP,64-31742,A etc.) or the direction of a molecule minor axis of the direction of a molecule minor axis are considered that SmC or chiral SmC phase organization potency is high from the data.

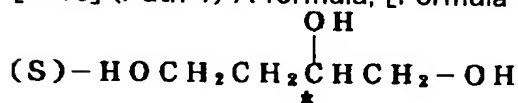
[0011] [Indication of invention] As for this invention person etc., the free rotation of the asymmetric carbon atom circumference is controlled by the above-mentioned various-views list based on consideration etc. The induction of the big spontaneous polarization can be carried out by arranging the sense of a dipole with an one direction. As a result of inquiring wholeheartedly by increasing the dimension height of the direction of a molecule minor axis paying attention to a chroman ring as skeletal structure considered that it can raise SmC nature or SmC* nature, or as a chiral dopant Or the effective compound as a presentation component required in the case of ferroelectric liquid crystal constituent production is found out, and it came to complete this invention. That is, this invention is a general formula [** 3].



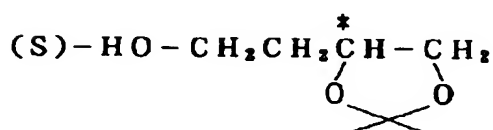
(R1 expresses the alkyl group of the carbon atomic numbers 1-5, and R2 expresses the alkyl group of the carbon atomic numbers 1-14.) k, l, and m express 0 or 1 independently, respectively. Z Single bond, -COO-, - either of CO- expressing -- X1 and X2 -- respectively -- independent -- a hydrogen atom or a fluorine atom -- expressing -- * -- an optical-activity carbon atom -- expressing -- offer the chroman derivative expressed and the liquid crystal constituent characterized by those things [containing a kind at least] at a list.

[0012] Although the new chroman derivative concerning this invention is compoundable in various paths, it **** the example below.

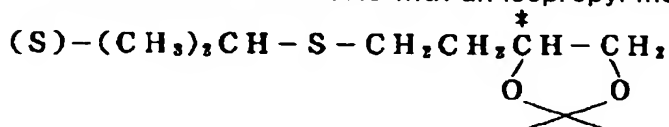
[0013] (Path 1) A formula, [Formula 4]



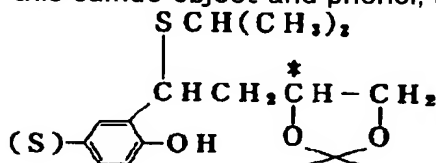
It comes out, ketal-ization according the compound (marketing) expressed to 3 and 3-dimethoxypropane is performed under existence of an acid catalyst, and they are a formula and [Formula 5].



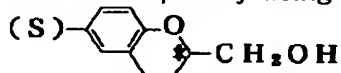
They are a formula and [Formula 6] by coming out, obtaining the compound expressed, making this into a tosylate object by p-toluenesulfonic-acid chloride, and making it react to the bottom of coexistence of NaOCH₃ with an isopropyl mercaptan further.



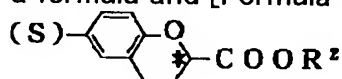
It comes out and the compound expressed is obtained. They are a formula and [Formula 7] by the ortho-alkylation reaction (J. Org.Chem., 1987, 52, 5495-5497) which passed through [2 by this sulfide object and phenol, and 3 sigmatropy transition.



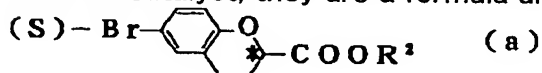
It comes out and the compound expressed is obtained. They are a formula and [Formula 8] by the dehydration perform deketal-ization under existence of the formation of deisopropyl thio which used the Raney nickel catalyst for this, and an acid catalyst, and in an alcoholic solution, and subsequently using the acid catalyst.



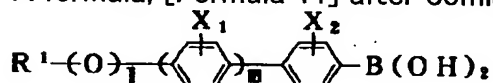
It comes out and the compound expressed is obtained. This thing is oxidized by the CrO₃/pyridine, an esterification reaction is further performed using alcohol (R²OH), and they are a formula and [Formula 9].



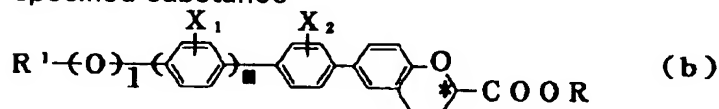
It comes out and the compound expressed is obtained. By the this bromination-reaction using a thallium catalyst, they are a formula and [Formula 10].



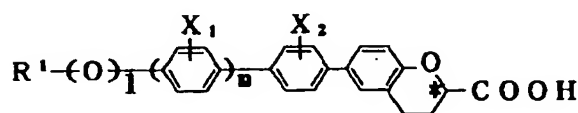
A formula, [Formula 11] after coming out and considering as the compound expressed



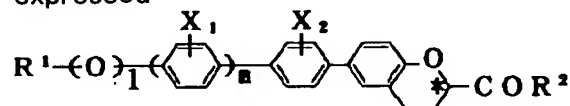
The formula, [Formula 12] which it comes out, and a coupling reaction is performed to the bottom of coexistence of the compound and Pd catalyst which are expressed, and are the specified substance



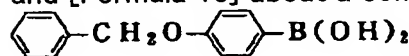
It comes out and the compound expressed is obtained. They are a formula and [Formula 13] by furthermore carrying out alkali hydrolysis of this about a compound (b).



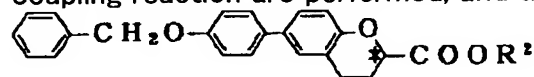
The formula, [Formula 14] which the reaction of this thing and Grignard reagent $R^2\text{MgBr}$ is made to perform, and are the specified substance after coming out and considering as the compound expressed



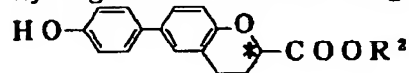
It comes out and the compound expressed is obtained. On the other hand, they are a formula and [Formula 15] about a compound (a).



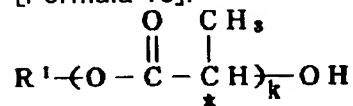
It comes out, the compound expressed, and the bottom of Pd catalyst coexistence and a coupling reaction are performed, and they are a formula and [Formula 16].



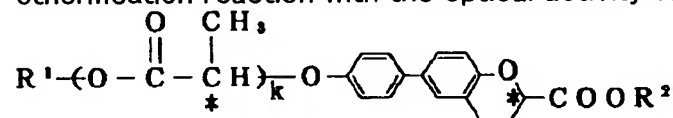
After coming out and considering as the compound expressed, this thing is debenzylated by the hydrogenation reaction using a Pd/C catalyst, and they are a formula and [Formula 17].



It comes out, the compound expressed is obtained and they are this thing, a formula, and [Formula 18].

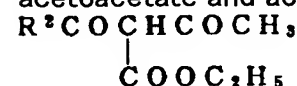


The formula, [Formula 19] which are the specified substance by coming out and making a etherification reaction with the optical activity alcohol expressed perform

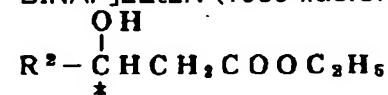


It comes out and the compound expressed is obtained.

[0014] (Path 2) They are a formula and [Formula 20] by performing the reaction of an ethyl acetoacetate and acyl chloride ($R^2\text{COCl}$) to the bottom of coexistence of MgOC_2H_5 .



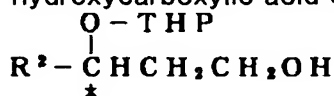
A formula and the compound of $R^2\text{COCH}_2\text{COOC}_2\text{H}_5$ are obtained by coming out, obtaining the compound expressed and deacetylating this under NaOC_2H_5 coexistence. They are beta-hydroxycarboxylic acid ethyl ester of optical activity, i.e., a formula, and [Formula 21] using this thing by making the asymmetric reduction (109 lit.J.Am.Chem.Soc.1987, 5856) using $\text{Ru}_2\text{Cl}_4[(R)\text{-BINAP}]_2\text{Et}_2\text{N}$ (1985 lit.J.Chem.Soc.Chem.Commun 922) perform.



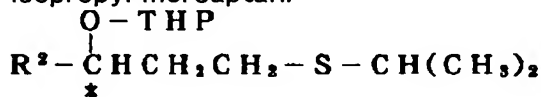
It comes out and the compound expressed is obtained. From said reference, this thing is

presumed that that absolute configuration is (R)-object.

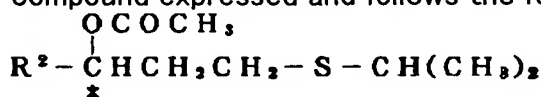
[0015] They are a formula and [Formula 22] by the reduction reaction protect OH of this beta-hydroxycarboxylic acid ethyl ester by tetrahydropyranyl (THP), and subsequently using LiAlH₄.



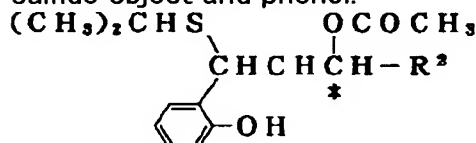
They are a formula and [Formula 23] by the reaction with the bottom of NaOCH₃ after coming out, obtaining compound expressed and using this thing as tosylate object3 coexistence, and an isopropyl mercaptan.



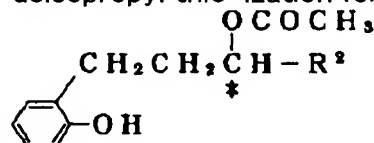
They are a formula and [Formula 24] by the acetylation reaction which comes out, obtains the compound expressed and follows the formation of deTHP and it by the acid in this.



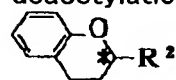
It comes out and considers as the compound expressed. They are a formula and [Formula 25] by the ortho-alkylation reaction which passed through [2, 3] sigmatropy transition reaction of this sulfide object and phenol.



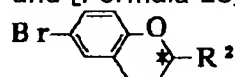
It comes out and the compound expressed is obtained. The Raney nickel catalyst performs deisopropyl thio-ization for this, and they are a formula and [Formula 26].



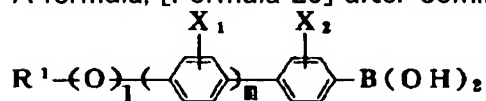
They are a formula and [Formula 27] by the dehydration ring closure reaction which follows the deacetylation and it by the acid after coming out and considering as the compound expressed.



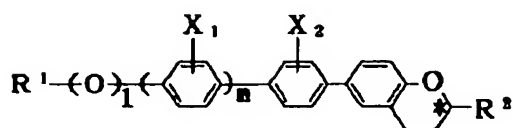
It comes out, the compound expressed is obtained, this is brominated, and they are a formula and [Formula 28].



A formula, [Formula 29] after coming out and considering as the compound expressed

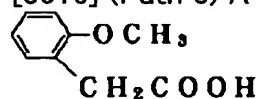


They are a formula and [Formula 30] by coming out and making a coupling reaction perform under existence of the compound and Pd catalyst which are expressed.

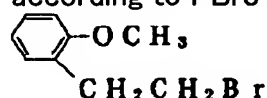


It comes out and the compound expressed is obtained. In addition, the absolute configuration of these optically active compounds is presumed to be (R)-object from the reaction path of solid maintenance.

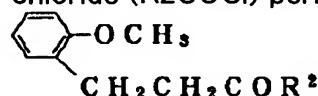
[0016] (Path 3) A formula, [Formula 31]



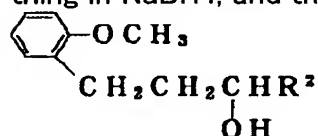
They are a formula and [Formula 32] by coming out and performing the reduction reaction according to the compound (marketing) expressed to LiAlH_4 , and the bromination reaction according to PBr_3 further.



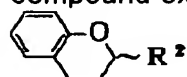
They are a formula and [Formula 33] by coming out, considering as the compound expressed, making this into a Grignard reagent with Mg , and subsequently making a reaction with acyl chloride (R_2COCl) perform.



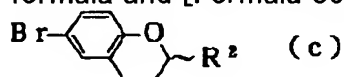
It comes out, the compound expressed is obtained, a reduction reaction is performed for this thing in NaBH_4 , and they are a formula and [Formula 34].



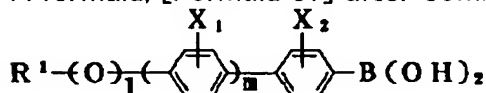
They are a formula and [Formula 35] by the ring closure reaction come out, consider as the compound expressed and according to a hydrobromic acid.



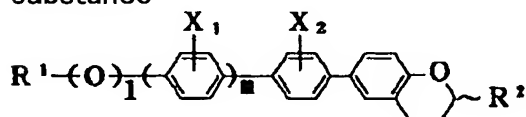
It comes out and considers as the compound expressed. This thing is brominated and they are a formula and [Formula 36].



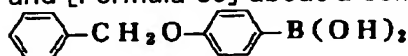
A formula, [Formula 37] after coming out and considering as the compound expressed



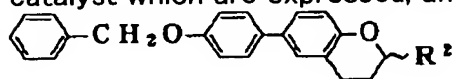
The formula, [Formula 38] which come out, and a coupling reaction is made to perform under existence of the compound and Pd catalyst which can be expressed, and are the specified substance



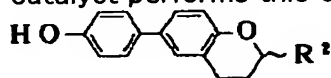
It comes out and the compound expressed is obtained. On the other hand, they are a formula and [Formula 39] about a compound (C).



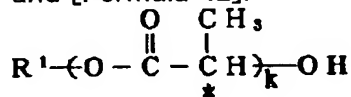
Come out, a coupling reaction is made to perform under existence of the compound and Pd catalyst which are expressed, and they are a formula and [Formula 40].



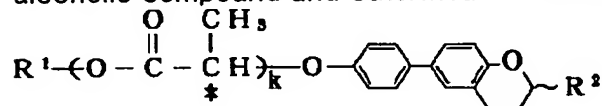
It comes out, the compound expressed is obtained, the hydrogenation reaction using a Pd-C catalyst performs this debenzoylation further, and they are a formula and [Formula 41].



It comes out, and considers as the compound expressed, and, subsequently they are a formula and [Formula 42].

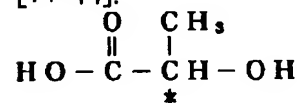


The formula, [Formula 43] which are the specified substance by coming out and making the alcoholic compound and etherification reaction which are expressed perform



It comes out and the compound expressed is obtained.

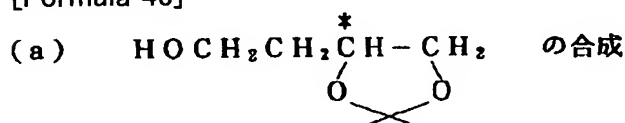
[0017] In addition, although, as for $k=1$ in a formula, $\text{R}^1=\text{CH}_3$, or the matter that is C_2H_5 , a commercial thing is used in the alcoholic above-mentioned compound, other matter is formulas [** 44].



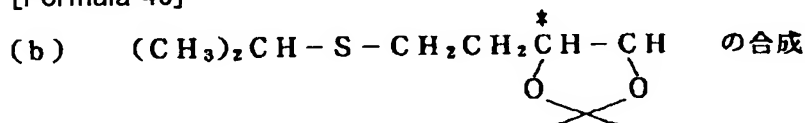
It is obtained using the alcohol which comes out and is expressed in formula $\text{R}^1\text{---OH}$ as the compound expressed by making an esterification reaction perform to the bottom of existence of a tosyl acid.

[0018] The example of this invention is hung up over below and this invention is explained still more concretely. In addition, since the phase transition temperature of the compound compound is influenced with the difference between measuring equipment and a measuring method, or purity, it will be understood that some difference is accepted in the numeric value.

[0019] The abridged notation indicated in the example has the meaning as follows.
the smectic phase SmB ; smectic B phase which was not made HPLC; high-performance-chromatography GC ; identification --- chiral SmC; chiral smectic C phase SmC ; smectic C phase [] SmA ---; smectic A phase Cho ; cholesteric phase Iso ; isotropy liquid ; Gas chromatography IR ; Infrared absorption spectrum GTO ; Glass tube oven bp. ; Boiling point mp. ; The melting point C ; Crystal SmX [0020] [Example 1]
[Formula 45]



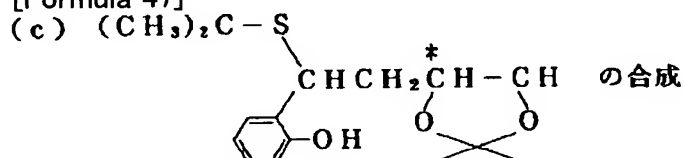
(S) - 1, 2, and 4-butane triol 50g (0.47M) was melted to acetone 800ml, and 0.4g (2mM) of p-toluenesulfonic-acid monohydrates was added. Subsequently, 2,2-dimethoxy propane 286ml was added and it was made to react under room temperature churning for 20 hours. NaHCO₃ 38.5g and 20ml were added after reaction termination, the solvent was distilled off after desiccation by Na₂SO₄, vacuum distillation of residue was carried out, and (S)-2 and 2-dimethyl -1 and 3-dioxolane-4-ethanol 69.2g was obtained. bp.50-56 degrees C /, 1torr, GC 74.9% [0021]
[Formula 46]



(S)-2 and 2-dimethyl -1 and 3-dioxolane-4-ethanol 69.2g obtained by (a) (0.47M) It melted to 450ml of methylene chlorides, and pyridine 100ml was added. P-toluenesulfonic-acid chloride 127g (0.66M) was added at 0 more degree C, and it agitated at this temperature for 1 hour. After leaving this reaction mixture in a refrigerator overnight, pouring, a methylene chloride extract, a saturation NaCl water solution, and water washed in water, the solvent was distilled off after desiccation by Na₂SO₄, and 142g of rough tosylate objects was acquired.

[0022] On the other hand, sodium 43g (1.87M) was melted to methanol 900ml, isopropyl mercaptan 172ml (1.84M) was added, and it agitated at the room temperature for 2 hours. Furthermore the methanol 150ml solution of a rough tosylate object was dropped, and it was made to react at 50 degrees C for 7 hours. The reaction mixture was poured into water, ether extract and rinsing were performed, after desiccation and a solvent were distilled off by Na₂SO₄, vacuum distillation of residue was carried out, and (S)-4-(2-isopropyl thio ethyl)-2 and 2-dimethyl -1 and 3-dioxolane 59.1g was obtained. bp.59-67 degree C/0.6 - 0.7torr, GC 93.2% [0023]

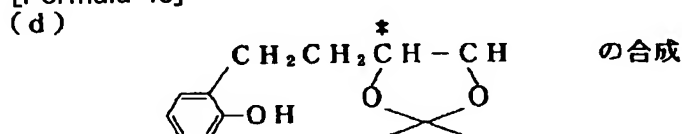
[Formula 47]



(S)-4-(2-isopropyl thio ethyl)-2 and 2-JIMECHIRU -1 and 3-dioxolane 20g (98mM) and S-collidine 17ml (0.12M) obtained by (b) were added to phenol 27.8g (0.29M) 200ml solution of methylene chlorides, the argon permutation of the system of reaction was carried out, and it cooled to -60 degrees C. Furthermore, 9.3ml (0.11M) of sulfuryl chlorides was dropped in the syringe, and after making it react for 15 minutes at this temperature, it was dropped so that the temperature of the system of reaction might keep triethylamine 80ml (0.65M) 80ml solution of methylene chlorides at -40 degrees C or less.

[0024] It poured into 1 N-HCl after reaction termination, the methylene chloride extract and saturation NaHCO₃ water solution washed, and it dried by Na₂SO₄, and after distilling off a solvent, from residue, the low-boiling point object was distilled in GTO, and (** S)-4-[2-(2-hydroxyphenyl)-2-isopropyl thio ethyl]-2 and 2-dimethyl -1 and 3-dioxolane 33g was obtained. GC 69.9% [0025]

[Formula 48]



The (** S)-4-[2-(2-hydroxyphenyl)-2-isopropyl thio ethyl]-2 which obtained 3 by (c) for 200ml ethanol 80cm of Raney nickel abbreviation, 2-dimethyl -1, and 3-dioxolane 16g (0.54M) ethanol 100ml solution was added, and reflux churning was carried out for 6 hours. Raney nickel was carried out the ** exception by heat filtration after reaction termination, filtrate was condensed,

residue was distilled in GTO, and (S)-4-[2-(2-hydroxyphenyl) ethyl]-2 and 2-dimethyl -1 and 3-dioxolane 7.4g was obtained. bp.115 degree C/0.2torr, GC 90.5%, $[\alpha]_{20D} = -45.5$ degree (c=2.51, CHCl₃)

[0026]

[Formula 49]

(e)



0.64g (3.3mM) of p-toluenesulfonic-acid monohydrates was added to the (S)-4-[2-(2-hydroxyphenyl)-ethyl]-2 and 2-dimethyl -1 and the 3-dioxolane 7.4g (33.3mM) methanol solution which were obtained by (d), and room temperature churning was carried out for 24 hours. after reaction termination and a solvent -- distilling off -- residue -- toluene 40ml -- and 0.64g (3.3mM) of p-toluenesulfonic-acid monohydrates was added again, and reflux churning was carried out for 9 hours using the water measuring tube. The reaction mixture was poured into water, the organic layer was isolated preparatively, the solvent was distilled off after desiccation by Na₂SO₄, residue was distilled in GTO, and (S)-chroman-2-methanol 2.9g was obtained. bp.110-125 degrees C /, 0.25torr, GC 89.0% [0027]

[Formula 50]

(f)



After adding CrO₃ 17g (0.17M) to 300ml of methylene chlorides, and the solution which consists of pyridine 35ml little by little and agitating at a room temperature for 10 minutes, 50ml solution of (S)-chroman-2-methanol 3.8g (23mM) methylene chlorides obtained by (e) was added, and room temperature churning was carried out for two days. The reaction mixture was poured into 1 N-NaOH, after ether washing, the water layer was made into acidity in dark HCl, the solvent was distilled off after desiccation by an ether extract, saturation NaCl water-solution washing, and Na₂SO₄, and 2.9g of (** S)-chroman-2-carboxylic acids was obtained. GC 96.2% [0028]

[Formula 51]

(g)



the ethanol 150ml solution of 2.7g of (S)-chroman-2-carboxylic acids obtained by (f) (15mM) -- dark -- H₂SO₄ 42ml was added and reflux churning was carried out for 7 hours. The solvent was condensed after reaction termination, the solvent was distilled off after desiccation by an ether extract, rinsing, and Na₂SO₄, residue was distilled in GTO, and (S)-chroman-2-carboxylic-acid ethyl ester 2.56g was obtained. bp.95-100 degrees C /, 0.2torr, GC97.2%, $[\alpha]_D = -5.6$ degree (c= 1.0, CHCl₃)

[0029]

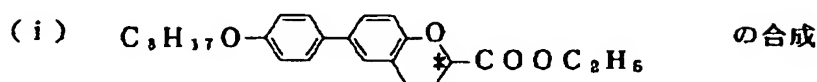
[Formula 52]

(h)



(S)-chroman-2-carboxylic-acid ethyl ester 2.47g 12mM obtained by (g) is melted to 20ml of methylene chlorides, the system of reaction is cooled at 0 degree C, and it is Ti(NO₃) 3.3H₂O. 0.62g (1.4mM) is added and it is Br₂ further. 0.36ml 10ml solution of methylene chlorides was dropped over 2 hours, and it agitated at 0 degree C for 1 hour. It poured into rare Na₂SO₃ water solution after reaction termination, the solvent was distilled off after desiccation by a methylene chloride extract, rinsing, and Na₂SO₄, residue was distilled in GTO, and (S)-6-BUROMO chroman-2-carboxylic-acid ethyl ester 2.2g was obtained. bp.115-120 degrees C /, 0.8torr, GC84.7% [0030]

[Formula 53]

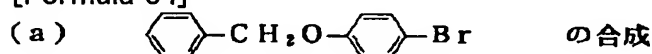


(S)-6-BUROMO chroman-2-carboxylic-acid ethyl ester 1g (3.5mM) the benzene 20ml solution, 2 M-Na2SO3 water solution, and 1.07g of 4-octyloxy phenyl boron acids obtained by (h) to Pd[Pph 3]4 of the amount of catalysts under N2 air current (3.85mM) The ethanol 10ml solution was added and reflux churning was carried out for 4 hours. It pours into water after reaction termination, a solvent is distilled off after desiccation by a benzene extract, rinsing, and Na2SO4, the silica gel column chromatography made into the eluate and recrystallization subsequently according to an acetone-ethanol mixed solvent refine residue for hexane-benzene (1:1), and it is (S)-6. -(4-octyloxy phenyl)- Chroman-2-carboxylic-acid ethyl ester 0.74g was obtained. [0031] It checked that the purity of this thing was 100% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 410 by IR and Mass analysis and a list was the specified substance.

[0032] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

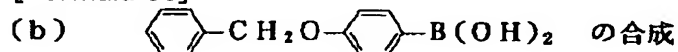
[0033] [Example 2]

[Formula 54]



Reflux churning of the mixture which consists of alpha-chloro toluene 25g (0.19M), 4-BUROMO phenol 27g (0.15M), K2CO3 51g (0.37M), and 2-butanone 300ml was carried out for 15 hours. The sludge was carried out the ** exception after reaction termination, the solvent was distilled off for filtrate after desiccation by a benzene extract, rinsing, and Na2SO4, residue was recrystallized with the hexane-methanol mixed solvent, and 4-benzyloxy bromobenzene 33.9g was obtained. GC98.2% [0034]

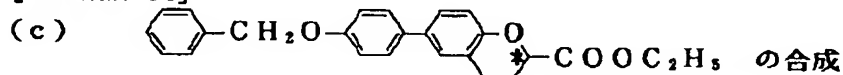
[Formula 55]



about [of the 4-benzyloxy bromobenzene 20g (76mM) THF100ml solution obtained by (a) to Mg2.03g (86.3mM) activated in I2 under N2 air current] -- 1/5 amount was applied and heated. The remaining THF solutions were dropped after reaction initiation, reflux churning was carried out for 1 hour, and the Grignard reagent was prepared.

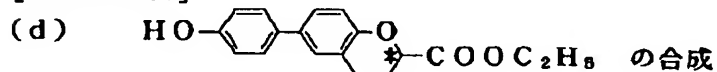
[0035] The Grignard reagent which cooled at 0-3 degrees C, and, on the other hand, prepared previously the THF20ml solution of 20g of trimethyl borate (0.15M) is dropped, and it returned to the room temperature and was made to react at 0 degree C for 1 hour for 1 hour. 10%H2SO4 water solution furthermore ice-cooled was dropped, the solvent was distilled off after desiccation by a benzene extract, rinsing, and Na2SO4, residue was recrystallized with the hexane-ether mixed solvent, and 7.66g of 4-benzyloxyphenyl boron acids was obtained. HPLC 91.5% [0036]

[Formula 56]



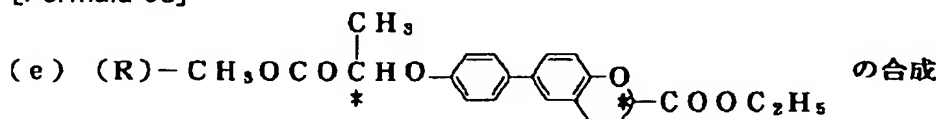
In example 1-(i), using 0.88g of 4-benzyloxyphenyl boron acids which changed to 1.07g of 4-octyloxy phenyl boron acids, and were obtained by (b), others were operated similarly and obtained (S)-6-(4-benzyloxyphenyl) chroman-2-carboxylic-acid ethyl ester 0.63g. HPLC 93.0%, MassM+298[0037]

[Formula 57]



(S)-6-(4-benzyloxyphenyl) chroman-2-carboxylic-acid ethyl ester 0.63g (1.6mM) and 20ml of

ethyl acetate obtained by 10%Pd/C of the amount of catalysts and (c) were taught to the autoclave, and room temperature churning was carried out for four days in hydrogen pressure 30atm. Pd/C was carried out the ** exception after reaction termination, the solvent was distilled off, and (** S)-6-(4-hydroxyphenyl) chroman-2-carboxylic-acid ethyl ester 0.43g was obtained. HPLC 99.4%, Mass M+298 [0038]
[Formula 58]



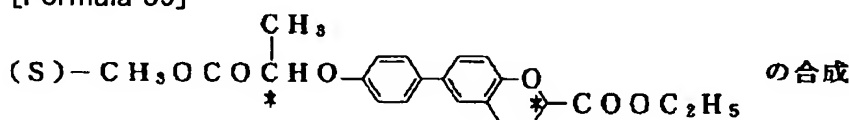
Azo dicarboxylic acid ethyl 0.33g (1.9mM) was dropped at the solution which consists of (S)-6-(4-hydroxyphenyl) chroman-2-carboxylic-acid ethyl ester 0.2g (0.6mM) obtained by (d), triphenylphosphine 0.36g (1.3mM), 0.21g (2.0mM) of (S)-methyl lactates, and THF20ml under ice-cooling churning, and it was made to react to it for seven days at a room temperature further. The solvent was distilled off after reaction termination, the silica gel chromatography which made benzene the eluate, and the preparative isolation thin-layer chromatography (20x20) which subsequently used the methylene chloride as the developing solution refined residue, and (R)-2-[4-((S)-2-ethoxycarbonyl chroman-6-IRU) phenoxy] propionic-acid methyl ester 95mg was obtained.

[0039] It checked that the purity of this thing was 98.4% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 384 by IR and Mass analysis and a list was the specified substance.

[0040] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

[0041] [Example 3]

[Formula 59]



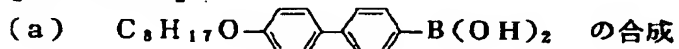
Changing to 0.21g of (S)-methyl lactates in example 2-(e), using (R)-methyl lactate, others were operated similarly and obtained (S)-2-[4-((S)-2-ethoxycarbonyl chroman-6-IRU) phenoxy] propionic-acid methyl ester 102mg.

[0042] It checked that the purity of this thing was 99.0% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 384 by IR and Mass analysis and a list was the specified substance.

[0043] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

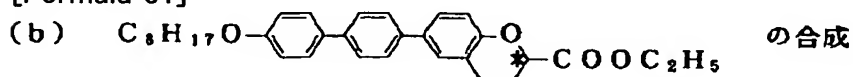
[0044] [Example 4]

[Formula 60]



Changing to 4-benzyloxy bromobenzene 20g in example 2-(b), using 4-octyloxy-4'-BUROMO biphenyl 27.4g, others were operated similarly and obtained 10.8g of 4-biphenyl-4'-boron acids. HPLC 84.2% [0045]

[Formula 61]



Using 1.25g of 4-octyloxy biphenyl-4'-boron acids which changed to 1.07g of 4-octyloxy phenyl boron acids in example 1-(i), and were obtained by (a), others were operated similarly and obtained (S)-6-(4-octyloxy biphenyl-4'-IRU) chroman-2-carboxylic-acid ethyl ester 0.53g.

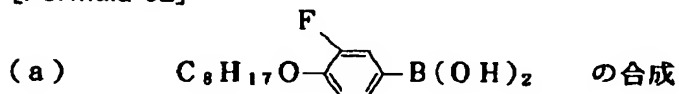
[0046] It checked that the purity of this thing was 98.7% in HPLC, and the matter obtained from

the raw material used for that the molecular ion peak was accepted in 486 by IR and Mass analysis and a list was the specified substance.

[0047] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

[0048] [Example 5]

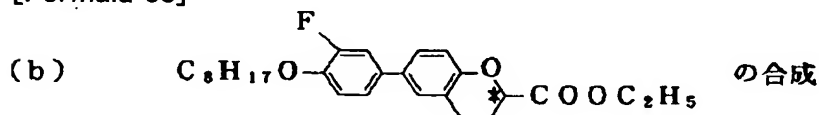
[Formula 62]



In example 2-(b), it changed to 4-benzyloxy bromobenzene 20g, and using 3-fluoro-4-octyloxy bromobenzene 23g, others were operated similarly and obtained 7.2g of 3-fluoro-4-octyloxy phenyl boron acids.

[0049]

[Formula 63]



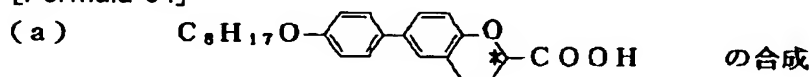
In example 1-(i), using 1.14g of 3-fluoro-4-octyloxy boron acids which changed to 1.07g of 4-octyloxy phenyl boron acids, and were obtained by (a), others were operated similarly and obtained (S)-6-(3-fluoro-4-octyloxy phenyl) chroman-2-carboxylic-acid ethyl ester 0.55g.

[0050] It checked that the purity of this thing was 99.8% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 428 by IR and Mass analysis and a list was the specified substance.

[0051] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

[0052] [Example 6]

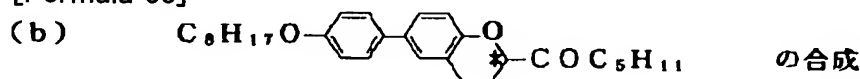
[Formula 64]



They are methanol 25ml and THF about (S)-6-(4-octyloxy phenyl) chroman-2-carboxylic-acid ethyl ester 0.3g (0.7mM) obtained by example 1-(i). It melted into the mixed liquor which consists of 10ml and 3ml of water, and NaOH0.21g (5.2mM) was added 95%, and reflux churning was carried out for 1 hour. It poured into water after reaction termination, and considered as acidity in dark HCl, the solvent was distilled off after desiccation by a benzene extract, rinsing, and Na2SO4, and 0.24g of (** S)-6-(4-octyloxy phenyl) chroman-2-carboxylic acids was obtained.

Mass M+382 [0053]

[Formula 65]



The bottom of N2 air current, Mg About 1/3 n-pentyl star's picture 1g (6.6mM) amount of an ether 20ml solution was applied and heated to 0.16g (6.6mM). The remaining ether solution was dropped after reaction initiation, reflux churning was carried out for further 1 hour, and the Grignard reagent was prepared.

[0054] On the other hand, the heating dissolution of the 0.24g (0.65mM) of the (S)-6-(4-octyloxy phenyl) chroman-2-carboxylic acids obtained by (a) was carried out in THF20ml under N2 air current, and screw (1, 3-diphenylphosphine propane) nickel (II) chloride was agitated for catalyst ***** 15 minutes after radiationnal cooling. Subsequently, the Grignard reagent prepared previously was dropped and room temperature churning was carried out for 12 hours. the silica gel column chromatography which poured into the rare HCl water solution after reaction termination, distilled off the solvent after desiccation by a benzene extract, rinsing, and Na2SO4,

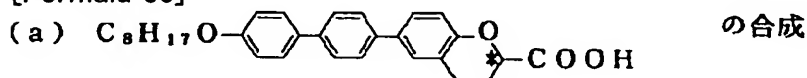
and made hexane-benzene (1:1) the eluate for residue -- subsequently recrystallization from a methanol-acetone mixed solvent refined, and (S)-6-(4-octyloxy phenyl)-2-hexa noil chroman 0.17g was obtained.

[0055] It checked that the purity of this thing was 99.1% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 436 by IR and Mass analysis and a list was the specified substance.

[0056] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

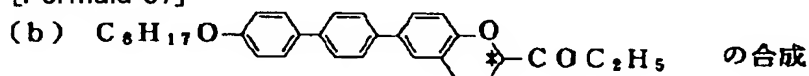
[0057] [Example 7]

[Formula 66]



The mixed liquor which consists of methanol 25ml, THF20ml, and 3ml of water is made to suspend (S)-6-(4-octyloxy biphenyl-4'-IRU) chroman-2-carboxylic-acid ethyl ester 0.25g (0.51mM) obtained by example 4-(b), and it is 95%NaOH. 0.2g (4.9mM) was added and heating churning was carried out for 30 minutes. The solvent was distilled off after reaction termination, water was added to residue, and it considered as acidity in dark HCl further, the sludge was separated and it rinsed, and after drying, 0.25g of (** S)-6-(4-octyloxy biphenyl-4'-IRU) chroman-2-carboxylic acids was obtained. MassM+458[0058]

[Formula 67]



The bottom of N2 air current, Mg To 0.22g (9.14mM), about 1/3 n-ethyl star's picture 1g (9.17mM) amount of an ether 20ml solution was applied and heated. The remaining ether solution was dropped after reaction initiation, reflux churning was carried out for further 2 hours, and the Grignard reagent was prepared.

[0059] On the other hand, the heating dissolution of the 0.24g (0.65mM) of the (S)-6-(4-octyloxy biphenyl-4'-IRU) chroman-2-carboxylic acids obtained by (a) was carried out in THF20ml under N2 air current, and screw (1, 3-diphenylphosphine propane) nickel (II) chloride was agitated for catalyst ***** 10 minutes after radiationnal cooling. Subsequently, the Grignard reagent prepared previously was dropped and room temperature churning was carried out for 30 hours. the silica gel column chromatography which poured into the rare HCl water solution after reaction termination, distilled off the solvent after desiccation by washing and Na2SO4 with an ether extract and ice-cooling water, and made benzene the eluate for residue, and preparative isolation thin-layer chromatography (20x20) -- subsequently recrystallization from an acetone refined and (S)-6-(4-octyloxy biphenyl-4'-IRU)-2-propanoyl chroman 73mg was obtained.

[0060] It checked that the purity of this thing was 99.8% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 470 by IR and Mass analysis and a list was the specified substance.

[0061] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

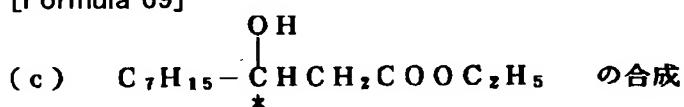
[0062] [Example 8]

[Formula 68]



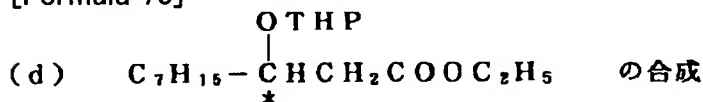
Mg When ethanol 34ml and 7ml of carbon tetrachlorides were added to 37.5g (1.54M) and it was left in the room temperature, the reaction began after several minutes, and reflux started. Benzene 140ml was dropped here, preparing so that the temperature of a system may become 60-70 degrees C, and the mixed liquor which subsequently consists of 200g [of acetoacetic ester] (1.54M) and ethanol 140ml and benzene 140ml was dropped so that the temperature of a

system might become 80 degrees C or less. It flowed back until the dropping termination back Mg melted completely. After cooling a reaction mixture radiationally to a room temperature, reaction temperature is kept at 30–35 degrees C on a water bath, and 1 hour was required, and the n-octanoyl chloride 227g (1.4M) benzene 210ml solution was dropped gradually, and was made to react at this temperature further for 2 hours. It diluted with 700ml of ice-cooling water after reaction termination, and considered as acidity in 30% H_2SO_4 water solution, and the benzene layer was isolated preparatively, the solvent was distilled off after desiccation by rinsing and Na_2SO_4 , vacuum distillation of residue was carried out, and ethyl n-octanoyl acetoacetate 253g was obtained. bp.120–123 degree C/0.9 – 1.5torr, GC 98.6% [0063] (b) Na_5g (0.21M) was melted to synthetic ethanol 140ml of $\text{C}_7\text{H}_{15}\text{COCH}_2\text{COOC}_2\text{H}_5$, ethyl n-octanoyl acetoacetate 250g (0.98M) obtained by (a) was added, and it boiled on the water bath for 4 hours. It poured into ice-cooling water after radiational cooling, and considered as acidity in 30% H_2SO_4 water solution, and the solvent was distilled off after desiccation by a benzene extract, rinsing, and Na_2SO_4 , vacuum distillation of residue was carried out, and ethyl n-octanoyl acetate 160g was obtained. bp.89–99 degrees C / , 0.3torr GC 95.6% [0064]
[Formula 69]

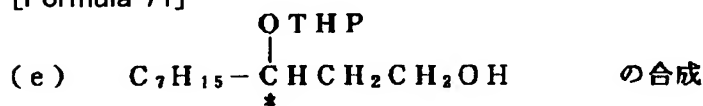


an autoclave -- $\text{Ru}_2\text{Cl}_4[(+)\text{-BINAP}]2\text{Et}_2\text{N}$ 1g, ethyl n-octanoyl acetate 110g (0.51M) obtained by (b), and ethanol 250ml were taught, and room temperature churning was carried out for one week in hydrogen pressure 100atm. The solvent was distilled off after reaction termination, vacuum distillation of residue was carried out, and 105g of optical activity ethyl beta-hydroxydecanoate was obtained. bp.89–108 degree C/0.3 – 0.4torr, GC 99%, o.p 99%ee, $[\alpha]_{\text{D}}^{19} = -5.37$ degree (neat)
[0065]

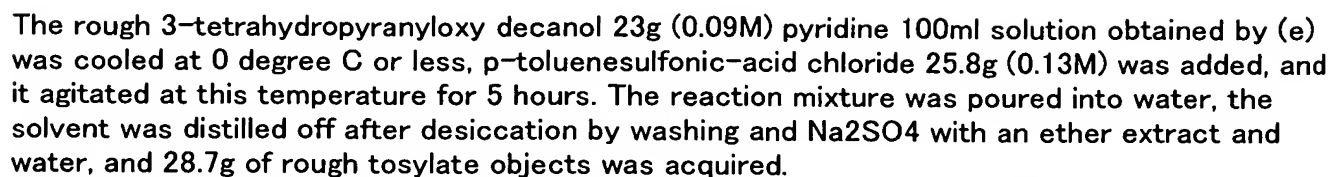
[Formula 70]



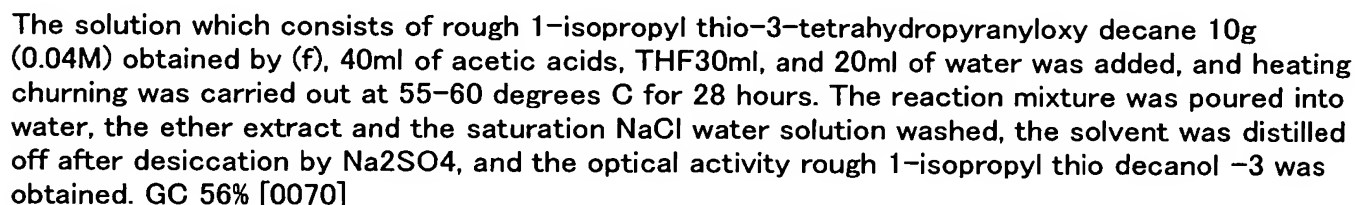
1.0g (4.1mM) of pyridinium p-toluenesulfonic acid was added to the solution which consists of ethyl beta-hydroxydecanoate [18] (83mM) and 3 and 4-dihydro-2H-pyran 10.5g (0.12M) and 180ml of methylene chlorides obtained by (c), and room temperature churning was carried out for 16 hours. NaHCO_3 solution and water washed 5% after reaction termination, the solvent was distilled off after Na_2SO_4 desiccation, and optical activity rough ethyl beta-tetrahydropyranyloxy decanoate 33.5g was obtained. GC 94.5% [0066]
[Formula 71]



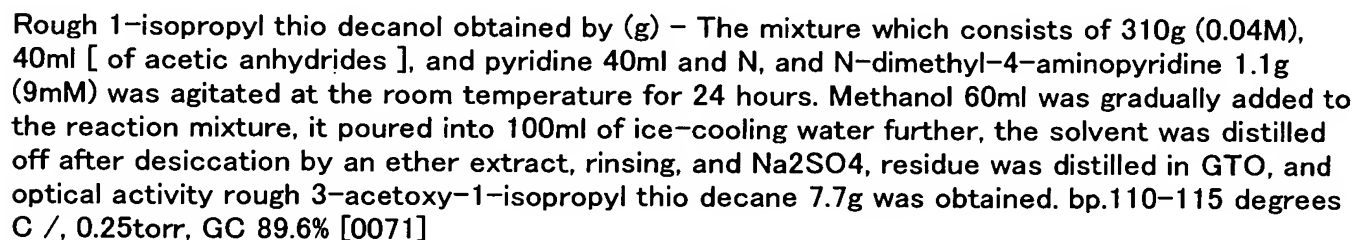
The bottom of ice-cooling churning, LiAlH_4 44.6g (0.12M), and rough ethyl beta-tetrahydropyranyloxy decanoate 33g obtained by (d) to the suspension which consists of ether 100ml (0.11M) It was dropped, and further, to the room temperature, the system of reaction was raised gradually and agitated for 5 hours. The system was cooled to –5 degrees C after reaction termination, and sequential dropping of 24ml [of ethyl acetate] and chloroform 160ml and the 24ml of the water was carried out. The sludge was carried out the ** exception, filtrate was distilled off in the saturation NaCl water solution, the solvent was distilled off after desiccation by washing and Na_2SO_4 , and optical activity 3-tetrahydropyranyloxy decanol 23.3g was obtained. GC96.1% [0067]
[Formula 72]



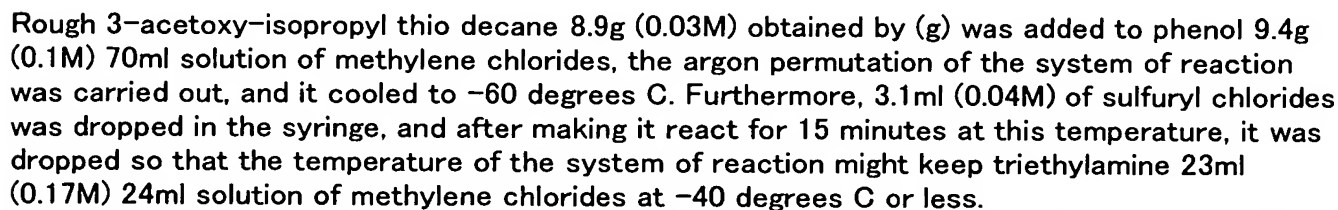
[Formula 73]



[Formula 74]

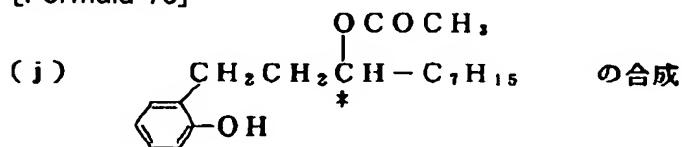


[Formula 75]

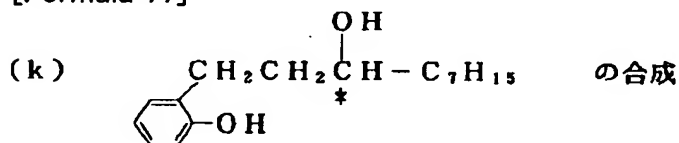


http://www4.ipdl.ncipi.go.jp/cgi-bin/tran_web.cgi_ejje

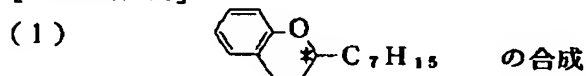
and optical activity rough 2-(3'-acetoxy-1'-isopropyl thio DESHIRU) phenol 3.05g was obtained. GC 72.1%, Mass M+466 [0073]
[Formula 76]



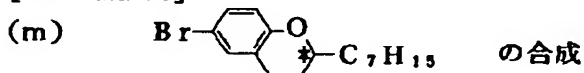
The rough 2-(3'-acetoxy-1'-isopropyl thio DESHIRU) phenol 3g (8.1mM) ethanol 25ml solution which obtained 3 by (i) for 25ml ethanol 24cm of Raney nickel abbreviation was added, and reflux churning was carried out for 19 hours. Raney nickel was carried out the ** exception by heat filtration after reaction termination, filtrate was condensed, and optical activity rough 2-(3'-acetoxy DESHIRU) phenol 2.37g was obtained. GC 51% [0074]
[Formula 77]



The rough 2-(3'-acetoxy DESHIRU) phenol 2.3g (0.01M) ether 30ml solution obtained by (j) was dropped at the suspension which consists of LiAlH43.0g (0.08M) and ether 70ml under ice-cooling churning, and the system of reaction was further raised gradually to the room temperature. It poured into the ice-cooled rare HCl water solution after reaction termination, the ether extract and the saturation NaCl water solution washed, the solvent was distilled off after desiccation by Na2SO4, and optical activity rough 2-(3'-hydroxy DESHIRU) phenol 1.87g was obtained. GC 51.3% [0075]
[Formula 78]

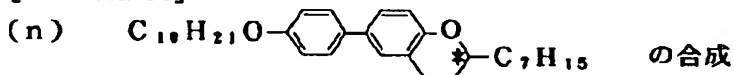


0.81g (4.3mM) of p-toluenesulfonic-acid monohydrates was added to the suspension which consists of rough 2-(3'-hydroxy DESHIRU) phenol 1.87g (7.5mM) obtained by (k), and benzene 50ml, and reflux churning was carried out for 8 hours. It poured into saturation NaHCO3 water solution after reaction termination, the solvent was distilled off for the organic layer after desiccation by rinsing and Na2SO4, and optical activity rough 2-heptyl chroman 1.59g was obtained. GC 58.5% [0076]
[Formula 79]



Rough 2-heptyl chroman 1.59g (5.1mM) 30ml solution of methylene chlorides obtained by (1) is cooled at 0 degree C, and it is Ti(NO3) 33H2O. 0.27g (0.6mM) was added, and further, 10ml solution of Br20.21 methylene chlorides of ml was required for 30 - 40 minutes, and was dropped.

[0077] It poured into rare Na2SO3 water solution after reaction termination, and the sludge was carried out the ** exception, filtrate was distilled off with the methylene chloride, the solvent was distilled off after desiccation by an extract, rinsing, and Na2SO4, residue was distilled in GTO, and optical activity rough 2-heptyl-6-BUROMO-chroman 0.78g was obtained. bp.160 degree C/0.7torr, GC 71.8%, Mass M+310, 312[0078]
[Formula 80]



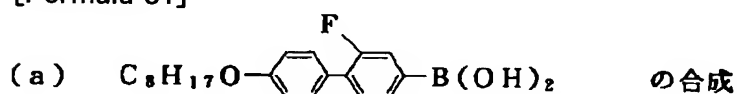
The 2-heptyl-6-BUROMO-chroman 0.5g (1.6mM) benzene 10ml solution obtained by (m), 2ml of 2 M-NaCO₃ water solutions, and the ethanol 5ml solution of 0.49g of 4-decyloxy phenyl boron acids (1.7mM) were added to Pd[PPh₃]₄ of the amount of catalysts under N₂ air current, and reflux churning was carried out for 6 hours. The silica gel column chromatography, 2-heptyl [optical activity / in the purification from an acetone-methanol mixed solvent / subsequently] -6 which poured into water after reaction termination, distilled off the solvent after desiccation by a benzene extract, rinsing, and Na₂SO₄, and made hexane-benzene (10:1) the eluate for residue -(4-decyloxy phenyl)- Chroman 0.27g was obtained. [alpha] 27D=-53.6 degree (c= 1, CHCl₃)

[0079] It checked that the purity of this thing was 97.7% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 465 by IR and Mass analysis and a list was the specified substance.

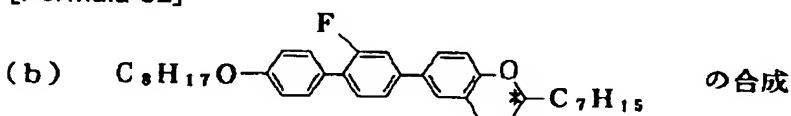
[0080] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

[0081] [Example 9]

[Formula 81]



Changing to 4-benzyloxy bromobenzene 20g in example 2-(b), using 2-fluoro-4'-octyloxy-4-BUROMO biphenyl 28.8g, others were operated similarly and obtained 9.9g of 2-fluoro-4'-octyloxy biphenyl-4-boron acids. HPLC 87.3% [0082]



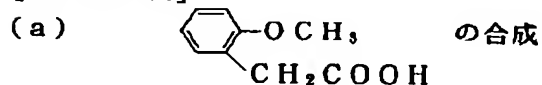
Using 0.6g of fluoro-4'-octyloxy biphenyl-4-boron acids which changed to 0.49g of 4-decyloxy phenyl boron acids in example 8-(n), and were obtained by (a), it is operated similarly and others are the optical activity 2-heptyl -6. -(2'-fluoro-4-octyloxy biphenyl-4-IRU)- Chroman 0.15g was obtained.

[0083] It checked that the purity of this thing was 97.2% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 530 by IR and Mass analysis and a list was the specified substance.

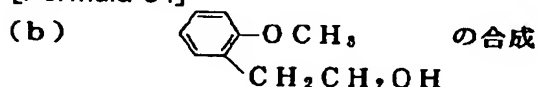
[0084] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 1 cited below.

[0085] [Example 10]

[Formula 83]



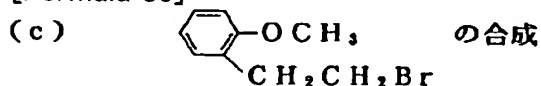
o-methoxyphenyl acetonitrile 299g (2.03M) is melted to methanol 500ml, and it is KOH 85%. 170g 200ml water solution of water was added, and reflux churning was carried out for two days until NH₃ smell was lost. It poured into the rare HCl water solution which ice-cooled the reaction mixture, the sludge was separated, ice-cooling water washed, reduced pressure drying was carried out further, and 319g of o-methoxypheny acetic acids was obtained. Mass M+166 [0086]



The THF200ml solution of 50g (0.3g) of o-methoxypheny acetic acids obtained by (a) was dropped at the suspension which consists of LiAlH₄15.6g (0.41M) and THF200ml under ice-

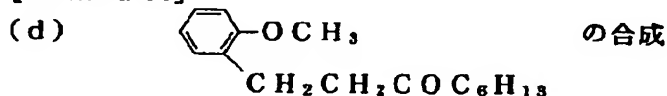
cooling churning, and further, to the room temperature, the system of reaction was raised gradually and agitated for 8 hours. The reaction mixture was poured into ice-cooling water, it considered as acidity in dark HCl, and rough 2-(o-methoxypheny) ethanol 46g was obtained after desiccation by washing and Na₂SO₄ in the ether extract and the saturation NaCl water solution. GC 99% [0087]

[Formula 85]



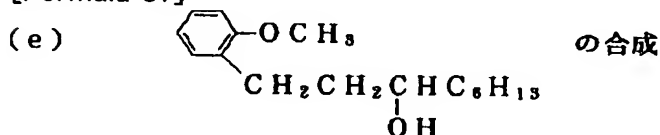
19g (0.06M) of phosphorus tribromide was dropped at 2-(o-methoxypheny) ethanol 20g (0.13M) 60ml solution of carbon tetrachlorides obtained by (b) at 0 degree C, and at 0 more degree C, it returned to the room temperature and agitated for 3 hours for 1 hour. The reaction mixture was poured into ice-cooling water, the solvent was distilled off after desiccation by an extract, rinsing, and Na₂SO₄ with the carbon tetrachloride, vacuum distillation of residue was carried out, and 2-(o-methoxypheny) ethyl star's picture 14.2g was obtained. bp.62-68 degrees C /, 0.3torr, GC 96.6% [0088]

[Formula 86]



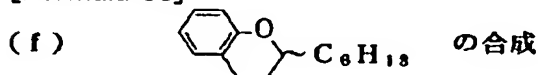
about [which added ether 40ml to Mg4.6g (18.9mM) under N₂ air current, and was further obtained by (c) / 2-(o-methoxypheny) ethyl star's picture 31.2g (0.14M) / of an ether 80ml solution] -- 1/3 amount was applied and heated, after reaction initiation, the remaining ether solution was dropped and reflux churning was carried out for 90 minutes. After cooling the system of reaction at 0 degree C and adding CdCl₂13.3g (73mM) small quantity every, reflux churning was carried out for 45 minutes. The ether was distilled out of the reaction mixture, benzene 90ml was added and it distilled off again, and benzene 100ml was added and the solvent permutation was carried out. After cooling radiationally to a room temperature, the hepta-noil chloride 19g (0.12M) benzene 10ml solution was dropped, and reflux churning was carried out for 40 minutes. The reaction mixture was poured into ice-cooling water, 80ml of rare H₂SO₄ water solutions was added, the organic layer was isolated preparatively, 50ml of 10 more%-NaOH-water-ethanol solutions was added after solvent distilling off, it diluted with water, desiccation and a solvent were distilled off by a benzene extract, rinsing, and Na₂SO₄, residue was distilled in GTO, and 2-(2-hepta-noil ethyl) anisole 19.5g was obtained. bp.135-140 degrees C /, 1.0torr, GC 78.3% [0089]

[Formula 87]



To the 2-(2-hepta-noil ethyl) anisole 19.4g (78.2mM) ethanol 150ml solution obtained by (d), it is NaBH₄. 3.5g (93mM) was added small quantity every, and room temperature churning was carried out for 4 hours. Ethanol was distilled out of the system of reaction, 100ml of water was added to residue, the solvent was distilled off after desiccation by washing and Na₂SO₄ in the ether extract and the saturation NaCl water solution, and rough 2-(3'-hydroxy nonyl) anisole 20.7g was obtained. GC 84.2% [0090]

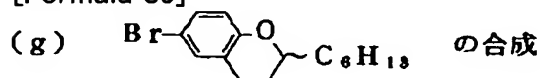
[Formula 88]



Rough 2-(3'-hydroxy nonyl) anisole 20g (91.7mM) obtained by (e), 100ml of acetic acids, 48%HBr Reflux churning of the mixture which consists of 150ml was carried out for 60 hours. the silica

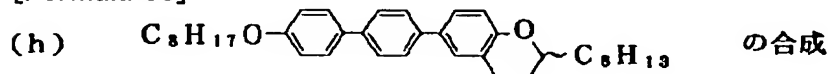
gel column chromatography which poured the reaction mixture into ice-cooling water, performed washing and rinsing one by one in an ether extract, rinsing, and a rare NaOH water solution, distilled off the solvent after desiccation by Na₂SO₄, and made the hexane the eluate for residue — subsequently it distilled in GTO and rough 2-hexyl chroman 3.8g was obtained. bp.95 degree C/0.6torr, GC 79.3% [0091]

[Formula 89]



Rough 2-hexyl chroman 3.6g (16.4mM) 30ml solution of methylene chlorides obtained by (f) is cooled at 0 degree C, and it is Ti(NO₃) 33H₂O. 0.84g (1.9mM) was added, and further, 10ml solution of methylene chlorides of Br₂ 1.3g (8.2mM) was required for 30 – 40 minutes, and was dropped. It poured into rare Na₂SO₃ water solution after reaction termination, and the sludge was carried out the ** exception, filtrate was distilled off with the methylene chloride, the solvent was distilled off after desiccation by an extract, rinsing, and Na₂SO₄, residue was distilled in GTO, and 2-hexyl-6-BUROMO chroman 2.7g was obtained. bp.135 degree C/0.7torr, GC 68.1% [0092]

[Formula 90]



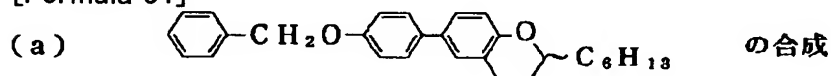
Pd of the bottom of N₂ air current, and the amount of catalysts -- [-- the 2-hexyl-6-BUROMO-chroman 1g (3.3mM) benzene 40ml solution obtained by (g) to pph34, 5ml of 2 M-NaCO₃ water solutions, and example 4- the ethanol 30ml solution of 1.2g of 4-octyloxy biphenyl boron acids obtained by (a) (3.7mM) was added, and reflux churning was carried out for 6 hours. the silica gel column chromatography which poured into water after reaction termination, distilled off the solvent after desiccation by a benzene extract, rinsing, and Na₂SO₄, and made the hexane-methylene chloride (5:1) the eluate for residue -- subsequently recrystallization was performed from the acetone and 2-hexyl-6-(4-octyloxy biphenyl-4'-IRU) chroman 0.44g was obtained.

[0093] It checked that the purity of this thing was 98.8% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 498 by IR and Mass analysis and a list was the specified substance.

[0094] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 5 cited below.

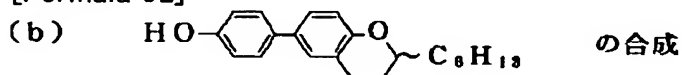
[0095] [Example 11]

[Formula 91]



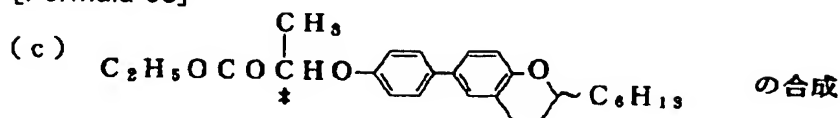
Using 0.84g of 4-benzyloxyphenyl boron acids which changed to 1.2g of 4-octyloxy biphenyl-4'-boron acids in example 10-(h), and were obtained by example 2-(b), others were operated similarly and obtained 2-hexyl-6-(4-benzyloxyphenyl) chroman 0.53g. HPLC 98.8%, Mass M+400 [0096]

[Formula 92]



2-hexyl-6-(4-benzyloxyphenyl) chroman 0.53g (1.3mM) and 25ml of ethyl acetate obtained by 10%Pd/C of the amount of catalysts and (a) were taught to the autoclave, and room temperature churning was carried out for four days in hydrogen pressure 35atm. Pd-C was carried out the ** exception after reaction termination, the solvent was distilled off, and 2-hexyl-6-(4-hydroxyphenyl) chroman 0.33g was obtained. HPLC 99.7%, Mass M+310 [0097]

[Formula 93]

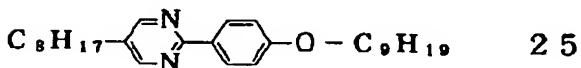
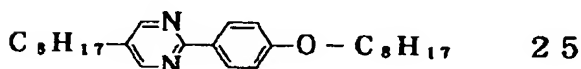
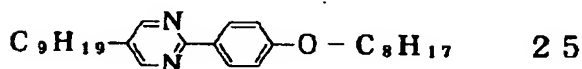
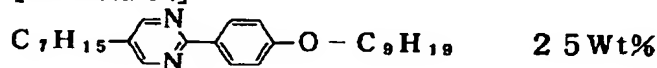


2-hexyl-6-(4-hydroxyphenyl) chroman 0.2g obtained by (b) (0.6mM) Azo dicarboxylic acid ethyl 0.33g (1.9mM) was dropped at the solution which consists of triphenyl REFSU fin 0.36g (1.3mM), 0.21g (2.0mM) of (S)-ethyl lactates, and THF20ml under ice-cooling churning, and it was made to react to it for seven days at a room temperature further, the silica gel column chromatography which distilled off the solvent after reaction termination and made the benzene-hexane (1:1) the eluate for residue -- subsequently recrystallization from a methanol refined and 99mg of (R)-2-[4-(2-hexyl chroman-6-IRU) phenoxy] ethyl propionate ester was obtained. [0098] It checked that the purity of this thing was 99.1% in HPLC, and the matter obtained from the raw material used for that the molecular ion peak was accepted in 410 by IR and Mass analysis and a list was the specified substance.

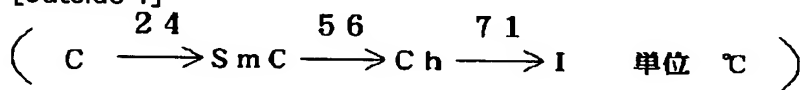
[0099] Phase transition temperature was observed for this thing under the polarization microscope with METORA hot stage FP-82. The result is shown in the table 4 cited below.

[0100] [Example 12]

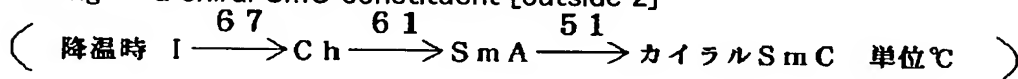
[Formula 94]



Parent liquid crystal which consists of the four above-mentioned sorts of pyrimidine compounds [outside 1]



It prepared. the compound obtained by this parent liquid crystal in the example 1 -- 5Wt(s)% -- adding -- a chiral SmC constituent [outside 2]



It prepared.

[0101] Polyimide spreading of this constituent was carried out, it poured into the liquid crystal cell of 2-micrometer gap created from the glass substrate with a transparent electrode which performed rubbing processing, and the liquid crystal device was created.

[0102] This liquid crystal device was inserted into two polarizing plates, the square wave (**5v [micrometer] /and 200Hz) was impressed, and the response time was found from change of transmitted light reinforcement. Moreover, spontaneous polarization was measured in the Sawyer testing orientation and work evaluation in rehabilitation, and whenever [tilt angle] was measured from the migration include angle of the extinction position at the time of the polarity reversals of applied voltage. The result is shown in the following table 1.

[0103]

[Table 1]

表 1

測定温度 (°C)	45	37	32	25
応答時間(μ s e c)	172	223	268	328
自発分極(nC/cm ²)	-2.8	-2.8	-3.7	-3.7
チルト角度 (°)	16.9	21.2	22.5	24.7

[0104] [an example 13] -- the compound which changed to the compound obtained in the example 1 in the example 12, and was obtained in the example 6 -- the same parent liquid crystal -- 5Wt(s)% -- the result of having measured whenever [tilt angle] in the response time and a spontaneous polarization list like the example 12 using the chiral SmC liquid crystal constituent added and created is shown below. In addition, the phase transition temperature at the time of the temperature fall of the created chiral SmC liquid crystal constituent (degree C) is [External Character 3].

6 6 6 4 4 6

I \longrightarrow C h \longrightarrow S m A \longrightarrow カイラル S m C

It came out.

[0105]

[Table 2]

表 2

測定温度 (°C)	43	36	31	25
応答時間(μ s e c)	173	221	284	482
自発分極(nC/cm ²)	-0.4	-0.9	-1.5	-1.5
チルト角度 (°)	7.2	10.2	12.4	14.1

[0106] [an example 14] -- the compound which changed to the compound obtained in the example 1 in the example 12, and was obtained in the example 11 -- the same parent liquid crystal -- 5Wt(s)% -- the result of having measured whenever [tilt angle] in the response time and a spontaneous polarization list like the example 12 using the chiral SmC liquid crystal constituent added and created is shown below. In addition, the phase transition temperature at the time of the temperature fall of the created chiral SmC liquid crystal constituent (degree C) is [External Character 4].

6 5 5 6 4 1

I \longrightarrow C h \longrightarrow S m A \longrightarrow カイラル S m C

It came out.

[0107]

[Table 3]

表 3

測定温度 (°C)	41	34	29	25
応答時間(μ s e c)	42	161	220	268
自発分極(nC/cm ²)	+1.3	+2.6	+2.6	+3.9
チルト角度 (°)	7.1	14.6	17.5	18.9

[0108]

[Table 4]

表 4

実施例 番 号	相転移温度 (°C)					
	C	SmX	カイラル SmC	SmA	Cho	Iso
1	• 76.8					•
2	• 87.8					•
3	• 63.7					•
4	• 146.5		• 158.2	• 189.7		•
5	• 58.3					•
6	• 80.4			(• 74.0)		•
7	• 130.5		• 152.2	• 228.4		•
8	• 67.2			• 93.4		•
9	• 71.9		• 123.5	• 159.6	• 173.2	•
11	• 38.1					•

[0109]

[Table 5]

表 5

実施例 番 号	相転移温度 (°C)					
	C	SmX	SmC	SmA	Cho	Iso
10	• 150.5		• 183.6	• 212.1		•

[Translation done.]

(19)日本国特許庁(JP)

(12)公開特許公報(A)

(11)特許出願公開番号

特開平5-25158

(43)公開日 平成5年(1993)2月2日

(51)Int.Cl. ⁵	識別記号	庁内整理番号	FI	技術表示箇所
C 0 7 D 311/04		6701-4C		
311/66		6701-4C		
C 0 9 K 19/42		6742-4H		
19/54	B	6742-4H		
19/58		6742-4H		

審査請求 未請求 請求項の数6(全 19 頁) 最終頁に続く

(21)出願番号	特願平3-273021	(71)出願人	591045677 関東化学株式会社 東京都中央区日本橋本町3丁目2番8号
(22)出願日	平成3年(1991)7月23日	(72)発明者	土屋 和彦 埼玉県草加市稲荷1-7-1 関東化学株式会社中央研究所内
		(72)発明者	杉浦 淳 埼玉県草加市稲荷1-7-1 関東化学株式会社中央研究所内
		(72)発明者	鈴木 賢治 埼玉県草加市稲荷1-7-1 関東化学株式会社中央研究所内
		(74)代理人	弁理士 安田 有三
			最終頁に続く

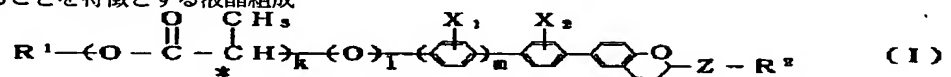
(54)【発明の名称】 クロマン誘導体並びにそれらを含む液晶組成物

(57)【要約】 (修正有)

物を提供する。

【目的】 新規な液晶性化合物並びにこれらの液晶性化合物の少なくとも1種を含有することを特徴とする液晶組成

【構成】 一般式

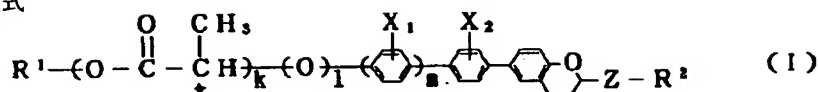


(R¹ は炭素原子数1~14のアルキル基を表し、R² は炭素原子数1~14のアルキル基を表し、k、l、m はそれぞれ独立に0または1を表し、Zは単結合、-COO-、-OCO-のいずれかを表し、X₁、X₂ はそれ

ぞれ独立に水素原子またはフッ素原子を表し、*は光学活性炭素原子を表す)で表されるクロマン誘導体並びにそれらのクロマン誘導体の少なくとも1種を含有する強誘電性液晶組成物。

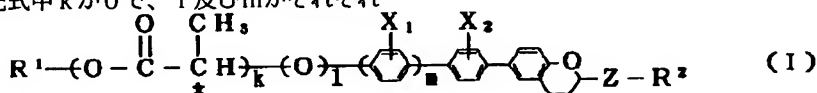
【特許請求の範囲】

【請求項1】 一般式



(R¹ は炭素原子数1～14のアルキル基を表し、R² は炭素原子数1～14のアルキル基を表し、k、l、m はそれぞれ独立に0または1を表し、Zは単結合、-C O-O-、-C O-のいずれかを表し、X₁、X₂ はそれぞれ独立に水素原子またはフッ素原子を表し、*は光学活性炭素原子を表す)で表されるクロマン誘導体。

【請求項2】 前記式中kが0で、l及びmがそれぞれ



(R¹ は炭素原子数1～14のアルキル基を表し、R² は炭素原子数1～14のアルキル基を表し、k、l、m はそれぞれ独立に0または1を表し、Zは単結合、-C O-O-、-C O-のいずれかを表し、X₁、X₂ はそれぞれ独立に水素原子またはフッ素原子を表し、*は光学活性炭素原子を表す)で表されるクロマン誘導体の少なくとも1種を含有することを特徴とする液晶組成物。

【請求項5】 前記式中kが0で、l及びmがそれぞれ独立に0または1で表される請求項4記載の液晶組成物。

【請求項6】 前記式中k及びlが1で、mが0または1で表される請求項4記載の液晶組成物。

【発明の詳細な説明】

【0001】〔技術分野〕本発明は、新規な液晶性化合物並びにこれらの液晶性化合物の少なくとも1種を含有することを特徴とする液晶組成物に関する。更に詳しく言えば、本発明は強誘電性液晶に関し、実用的な強誘電性液晶組成物作製の際、その組成成分として有用で且つ化学的安定性に優れた新規なクロマン骨格を有する液晶性化合物並びに、それらの新規なクロマン骨格を有する液晶性化合物の少なくとも1種を含有する液晶組成物に関する。

【0002】〔背景技術〕時計、電卓、パーソナルワープロ、ポケットテレビ用等の表示素子として、液晶表示素子は広く用いられている。これは受光型で目が疲れない、消費電力が少ない、薄型である等の優れた特徴を有しているためであるが、一方においては応答速度が遅い、メモリー性がない等から応用面に於いて制限があった。応用面の拡大を図るため、従来用いられていたツイステッドネマチック(TN)型表示方式を改良したスーパーツイステッドネマチック(STN)型表示方式等も見いだされている。しかし、これらは大画面表示或いはグラフィック表示用としては充分ではなく、これらに代わる液晶表示素子の研究も種々行われている。

【0003】その1つに強誘電性液晶[R. B. Me y 50

独立に0または1で表される請求項1記載のクロマン誘導体。

【請求項3】 前記式中k及びlが1で、mが0または1で表される請求項1記載のクロマン誘導体。

【請求項4】 一般式

(化2)

er 5; Physique, 36 L-69 (1975)] を利用した表示方式[N. A. Clark 5; Applied Phys. Lett., 36, 899 (1980)]がある。

【0004】この方式は従来方式に比べ1000倍もの高速応答であること、及びメモリー性があること等の優れた特徴を有しているため、液晶表示素子の用途拡大が期待されている。強誘電性液晶は、液晶分子長軸が層法線方向とある角度を有するスメクチック液晶を指すが、中でも実用的にはカイラルスメクチックC(カイラルSmC)相が用いられる。

【0005】表示素子作製用の強誘電性液晶は、(1)種々のカイラルSmC相を有する化合物同士、又は、

(2)種々のSmC相を有する化合物と光学活性化合物とを混合して得られる液晶組成物として用いられる。強誘電性液晶表示素子の研究開発は当初(1)の方式で得られる液晶組成物を用いていたが、研究開発が進捗し、SmC相を有する化合物に光学活性化合物を添加することにより強誘電性液晶が得られることが判明して以来、

(2)の方式で得られる組成物を用いる方向にある。【0006】特にSmC化合物を混合して得られるSmC組成物(SmCホスト)に1種～数種の光学活性化合物(カイラルSmC相を有している方が良いが、必ずしも有していなくともよい化合物でキラルドーパントと称される)を添加して強誘電性液晶組成物を作製する方法が主流となってきている。

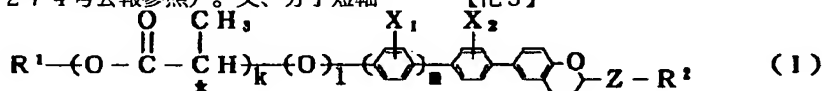
【0007】これは実用面に於て、(2)の方が市場から要求される種々の特性(動作温度範囲、応答速度、自発分極、ラセンピッチ、化学的安定性等)を調整しやすいこと、又、カイラルSmC化合物に比べてSmC化合物は安価に合成できること等から(2)が有利と考えられているためである。しかし、未だ実用に供せられるに至っておらず、強誘電性液晶組成物作製の際に有用な成分となりうる化合物の開発が望まれている。

【0008】キラルドーパントに要求される特性の1つ

に、SmCホストにそれを添加することにより得られる強誘電性液晶組成物の自発分極が大きいことが上げられる。

【0009】これは強誘電性液晶における応答時間と自発分極の関係式 $\tau = \eta / P_s \cdot E$ (τ = 応答時間、 η = 粘性、 E = 電界、 P_s = 自発分極) から明らかなように、自発分極を大きくすれば応答時間を短くできるためである。

【0010】自発分極とキラルドーパントの分子構造との関係については、諸説あるものの経験則の域を脱しておらず、未だ確固としたものはないが、それらの中の1つに「強誘電性を発現させる分子構造中の双極子モーメントを持つ部分の自由回転を抑制できれば、全体としての双極子部分を一定の方向に向かわせることが可能となり、自発分極を大きくすることができる」との説がある(特開平2-138274号公報参照)。又、分子短軸

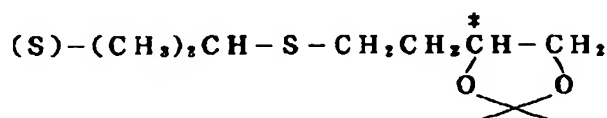


(R^1 は炭素原子数1~5のアルキル基を表し、 R^2 は炭素原子数1~14のアルキル基を表し、 k 、 l 、 m はそれぞれ独立に0または1を表し、 Z は単結合、 $-COO-$ 、 $-CO-$ のいずれかを表し、 X_1 、 X_2 はそれぞれ独立に水素原子またはフッ素原子を表し、*は光学活性炭素原子を表す) で表されるクロマン誘導体、並びにそれらの少なくとも一種を含有することを特徴とする液晶組成物を提供するものである。

【0012】本発明に係る新規なクロマン誘導体は、種々の経路で合成することができるがその例を以下に式示す。

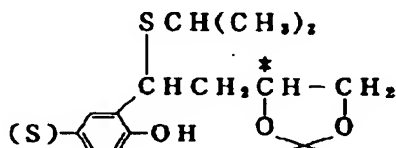
【0013】(経路1) 式、

【化4】



で表される化合物を得る。このスルフィド体とフェノールによる〔2, 3〕シグマトロピー転移を経たortho-アルキル化反応(J. Org. Chem., 1987, 52, 5495~5497)により、式、

【化7】



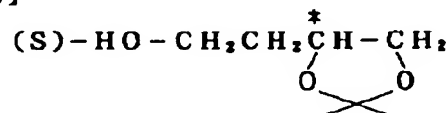
方向の嵩高さの大きいナフタレン誘導体(特開昭64-31742号公報等)あるいは分子短軸方向にハロゲン原子を導入した化合物(特開平1-250335号公報等)はそのデータからSmCまたはカイラルSmC相形成能が高いと考えられている。

【0011】〔発明の開示〕本発明者等は、上記の諸説並びに考察等を基に不斉炭素原子周辺の自由回転が抑制され、双極子の向きが一方向にそろえられることによって大きな自発分極が誘起できる、あるいは分子短軸方向の嵩高さを増すことでSmC性またはSmC*性を高めることができると考えられる骨格構造としてクロマン環に着目し、鋭意研究した結果、キラルドーパントとして、あるいは強誘電性液晶組成物作製の際に必要な組成成分として有効な化合物を見出し、本発明を完成するに至った。すなわち本発明は、一般式

【化3】

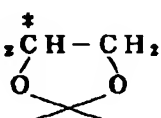
で表される化合物(市販)を酸触媒の存在下、3, 3-ジメトキシプロパンによるケタール化を行い、式、

【化5】



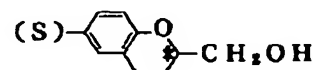
で表される化合物を得、これをp-トルエンスルホンクロライドによりトシレート体とし、さらにNaOCH₃の共存下に、イソプロピルメルカプタンと反応させることにより、式、

【化6】



で表される化合物を得る。これをラネーNi触媒を用いた脱イソプロピルチオ化及び酸触媒の存在下、アルコール溶液中にて脱ケタール化を行い、次いで酸触媒を用いた脱水反応により、式、

【化8】

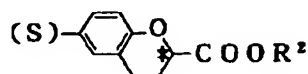


で表される化合物を得る。このものをCrO₃/ピリジンにより酸化し、さらにアルコール(R²OH)を用い

5

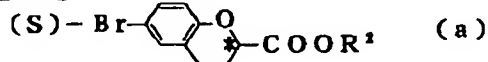
て、エステル化反応を行い、式、

【化9】

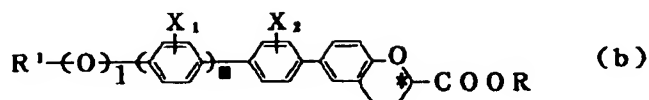


で表される化合物を得る。これをタリウム触媒を用いた臭素化反応により、式、

【化10】

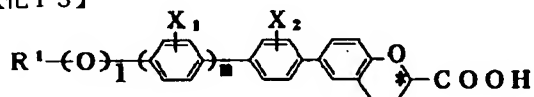


10



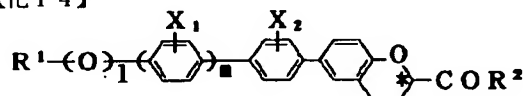
で表される化合物を得る。さらに化合物 (b) については、これをアルカリ加水分解することにより式、

【化13】



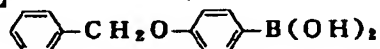
で表される化合物とした後、このものとグリニヤール試薬 $\text{R}^2 \text{MgBr}$ との反応を行わせ、目的物である式、

【化14】

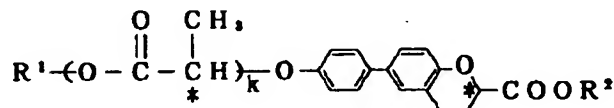


で表される化合物を得る。一方、化合物 (a) を式、

【化15】



で表される化合物と Pd 触媒共存下、カップリング反応を行い式、



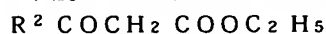
で表される化合物を得る。

【0014】(経路2) MgOC_2H_5 の共存下、アセト酢酸エチルとアシルクロライド ($\text{R}^2 \text{COCl}$) との反応を行うことにより式、

【化20】



で表される化合物を得、これを NaOC_2H_5 共存下に、脱アセチル化することにより、式、



6

で表される化合物とした後、式、

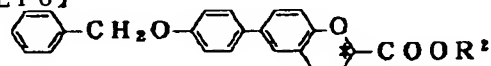
【化11】



で表される化合物と Pd 触媒の共存下に、カップリング反応を行い、目的物である、式、

【化12】

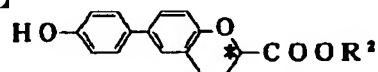
【化16】



20

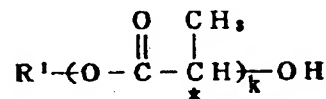
で表される化合物とした後、Pd/C 触媒を用いた水添反応によりこのものの脱ベンジル化を行い式、

【化17】



で表される化合物を得、このものと式、

【化18】



で表される光学活性なアルコールとのエーテル化反応を行わせることにより、目的物である式、

【化19】

40

の化合物を得る。このものを用いて、 $\text{Ru}_2\text{Cl}_4[(R)-\text{BINAP}]_2\text{Et}_2\text{N}$ (lit. J. Chem. Soc. Chem. Commun. 1985, 922) を用いた不斉還元 (lit. J. Am. Chem. Soc. 1987, 109, 5856) を行わせることにより、光学活性の β -ヒドロキシカルボン酸エチルエステルすなわち、式、

【化21】



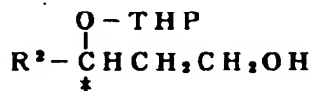
50

7

で表される化合物を得る。このものは前記文献より、その絶対配置は (R) 一体であると推定される。

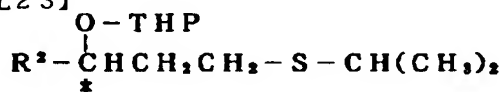
【0015】このβ-ヒドロキシカルボン酸エチルエステルのOHをテトラヒドロピラン (THP) で保護し、次いでLiAlH₄を用いた還元反応により式、

【化22】



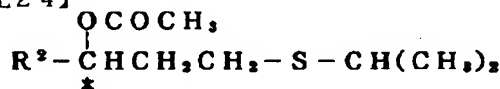
で表される化合物を得、このものをトシレート体とした後、NaOCH₃ 共存下、イソプロピルメルカプタンとの反応により式、

【化23】



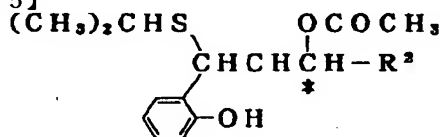
で表される化合物を得、これを、酸による脱THP化とそれに続くアセチル化反応とにより式、

【化24】



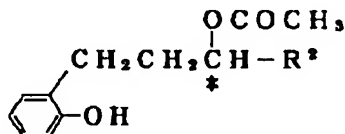
で表される化合物とする。このスルフィド体とフェノールとの〔2, 3〕シグマトロピー転移反応を経たortho-アルキル化反応により式、

【化25】



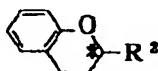
で表される化合物を得る。これをラネーNi触媒により、脱イソプロピルチオ化を行い式、

【化26】



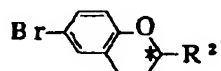
で表される化合物とした後、酸による脱アセチル化とそれに続く脱水閉環反応とにより式、

【化27】



で表される化合物を得、これを臭素化して式、

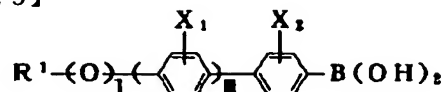
【化28】



8

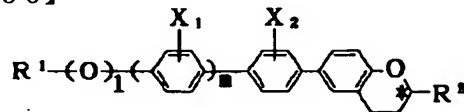
で表される化合物とした後、式、

【化29】



で表される化合物とPd触媒の存在下でカップリング反応を行わせることにより式、

【化30】



で表される化合物を得る。なお、これらの光学活性化合物の絶対配置は、立体保持の反応経路より、(R) 一体であると推定される。

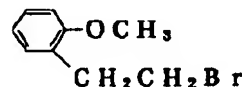
【0016】(経路3) 式、

【化31】



で表される化合物(市販)をLiAlH₄による還元反応と、さらにPBr₃による臭素化反応とを行うことにより式、

【化32】



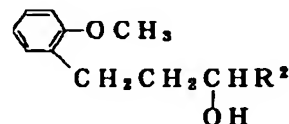
で表される化合物とし、これをMgによりグリニヤール試薬とし、次いで、アシルクロライド(R²COCl)との反応を行わせることにより式、

【化33】



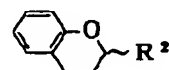
で表される化合物を得、このものをNaBH₄にて還元反応を行い式、

【化34】



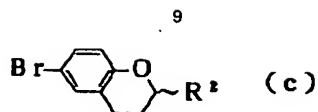
で表される化合物とし、これを臭化水素酸による閉環反応により式、

【化35】



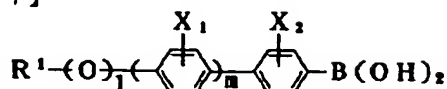
で表される化合物とする。このものを臭素化して式、

【化36】



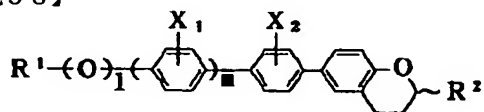
で表される化合物とした後、式、

【化37】



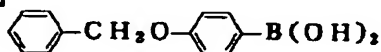
で表せられる化合物とPd触媒の存在下でカップリング反応を行わせ、目的物である式、

【化38】



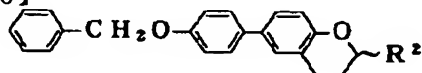
で表される化合物を得る。一方、化合物(c)を、式、

【化39】



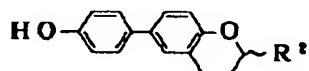
で表される化合物とPd触媒の存在下でカップリング反応を行わせ、

【化40】



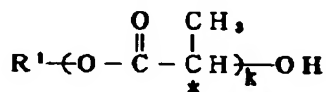
で表される化合物を得、さらにPd-C触媒を用いた水添反応によりこの脱ベンジル化を行い、式、

【化41】



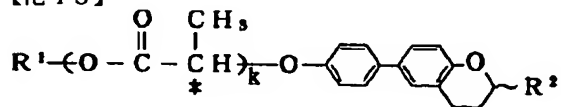
で表される化合物とし、次いで、式、

【化42】



で表されるアルコール化合物とエーテル化反応を行わせることにより、目的物である式、

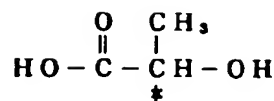
【化43】



で表される化合物を得る。

【0017】なお、上記のアルコール化合物において、式中のk=1、R1=CH3、又はC2H5である物質は、市販のものが使用されるがその他の物質は、式

【化44】



で表される化合物と式R1-OHで表されるアルコールとを用い、トシル酸の存在下に、エステル化反応を行わせることにより得られる。

【0018】以下に本発明の実施例を掲げ、本発明をさらに具体的に説明する。なお、合成した化合物の相転移温度は測定機器、測定方法の違い、或いは純度により影響されるため、その数値に多少の異同が認められることは理解されよう。

【0019】実施例中に記載されている略記号は以下のとおりの意義を有する。

HPLC ; 高速液体クロマトグラフィー

GC ; ガスクロマトグラフィー

IR ; 赤外線吸収スペクトル

GTO ; ガラスチューブオープン

b.p. ; 沸点

mp. ; 融点

C ; 結晶

SmX ; 同定できなかったスメクチック相

SmB ; スメクチックB相

カイラルSmC ; カイラルスメクチックC相

SmC ; スメクチックC相

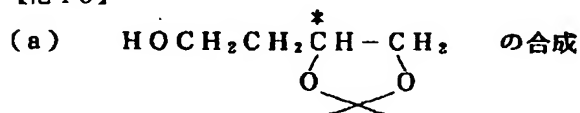
SmA ; スメクチックA相

Cho ; コレステリック相

Iso ; 等方性液体

【0020】【実施例1】

【化45】



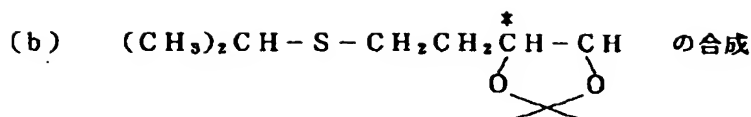
(S)-1, 2, 4-ブタントリオール50g (0.47M)をアセトン800mlに溶かし、p-トルエンスルホン酸一水和物0.4g (2mM)を加えた。次いで、室温攪拌下、2, 2-ジメトキシプロパン286mlを加え20時間反応させた。反応終了後、NaHCO3 8.5g及び20mlを加え、Na2SO4にて乾燥後、溶媒を留去し、残留分を減圧蒸留し、(S)-2, 2-ジメチル-1, 3-ジオキソラン-4-エタノール69.2gを得た。b.p. 50~56℃/1 torr、GC 74.9%

【0021】

【化46】

11

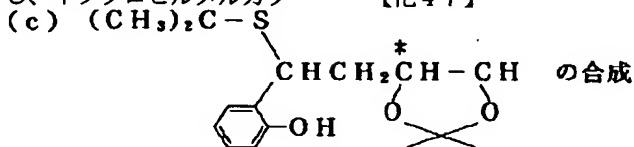
12



(a) で得た (S)-2, 2-ジメチル-1, 3-ジオキソラン-4-エタノール 69.2 g (0.47 M) を塩化メチレン 450 ml に溶かし、ピリジン 100 ml を加えた。さらに 0℃ にて p-トルエンスルホン酸クロライド 127 g (0.66 M) を加え 1 時間同温度にて攪拌した。この反応混合物を冷蔵庫にて一晩放置した

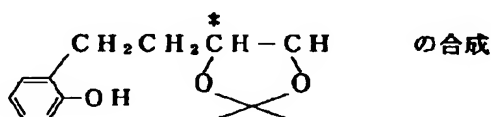
後、水に注加、塩化メチレン抽出、飽和 NaCl 水溶液及び水にて洗浄を行い、Na₂SO₄ にて乾燥後、溶媒を留去し、粗トシレート体 142 g を得た。

【0022】一方、メタノール 900 ml にナトリウム 43 g (1.87 M) を溶かし、イソプロピルメルカプ



フェノール 27.8 g (0.29 M) の塩化メチレン 200 ml 溶液に (b) で得た (S)-4-(2-イソプロピルチオエチル)-2, 2-ジメチル-1, 3-ジオキソラン 20 g (98 mM) 及び S-コリジン 17 ml (0.12 M) を加え、反応系をアルゴン置換し、-60℃ まで冷却した。さらに、塩化スルフル 9.3 ml (0.11 M) をシリンジにて滴下し、同温度にて 15 分間反応させた後、トリエチルアミン 80 ml (0.65 M) の塩化メチレン 80 ml 溶液を反応系の温度が -40℃ 以下に保つように滴下した。

(d)



ラネー Ni 約 80 cm³ を 200 ml のエタノールにとり、(c) で得た粗 (S)-4-[2-(2-ヒドロキシフェニル)-2-イソプロピルチオエチル]-2, 2-ジメチル-1, 3-ジオキソラン 16 g (0.54 M) のエタノール 100 ml 溶液を加え、6 時間還流攪拌した。反応終了後、熱濾過にてラネー Ni を濾別し、濾液を濃縮し、残留分を GTO にて蒸留し、(S)-4-[2-(2-ヒドロキシフェニル)エチル]-2, 2-ジメチル-1, 3-ジオキソラン 7.4 g を得た。b.p. 115℃/0.2 torr, GC 90.5%, [α]_D²⁰ = -45.5° (c=2.51, CHCl₃)

【0026】

【化49】

タン 172 ml (1.84 M) を加え、室温にて 2 時間攪拌した。さらに粗トシレート体のメタノール 150 ml 溶液を滴下し、50℃ にて 7 時間反応させた。反応混合物を水に注加し、エーテル抽出、水洗を行い、Na₂SO₄ にて乾燥後、溶媒を留去し残留分を減圧蒸留し、(S)-4-(2-イソプロピルチオエチル)-2, 2-ジメチル-1, 3-ジオキソラン 59.1 g を得た。b.p. 59~67℃/0.6~0.7 torr, GC 93.2%

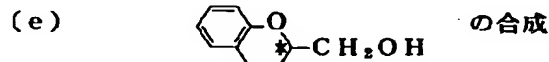
【0023】

【化47】

【0024】反応終了後、1N-HCl に注加し、塩化メチレン抽出、飽和 NaHCO₃ 水溶液にて洗浄を行い、Na₂SO₄ にて乾燥し、溶媒を留去後、残留分より低沸点物を GTO にて蒸留し、粗 (S)-4-[2-(2-ヒドロキシフェニル)-2-イソプロピルチオエチル]-2, 2-ジメチル-1, 3-ジオキソラン 33 g を得た。GC 69.9%

【0025】

【化48】

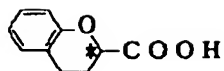


(d) で得た (S)-4-[2-(2-ヒドロキシフェニル)エチル]-2, 2-ジメチル-1, 3-ジオキソラン 7.4 g (33.3 mM) のメタノール溶液に p-トルエンスルホン酸一水和物 0.64 g (3.3 mM) を加え、24 時間室温攪拌した。反応終了後、溶媒を留去し、残留分にトルエン 40 ml 及び再度 p-トルエンスルホン酸一水和物 0.64 g (3.3 mM) を加え、検水管を用いて 9 時間還流攪拌した。反応混合物を水に注加し、有機層を分取し、Na₂SO₄ にて乾燥後、溶媒を留去し、残留分を GTO にて蒸留し、(S)-クロマン-2-メタノール 2.9 g を得た。b.p. 110~125℃/0.25 torr, GC 89.0%

【0027】

【化50】

(f)



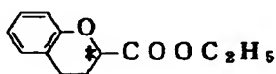
の合成

塩化メチレン300mlとピリジン35mlから成る溶液にCrO₃ 17g (0.17M)を少しずつ加え、10分間室温にて攪拌した後、(e)で得た(S)-クロマン-2-メタノール3.8g (23mM)塩化メチレン50ml溶液を加え、2日間室温攪拌した。反応混合物を1N-NaOHに注加し、エーテル洗浄後、濃HClにて水層を酸性にしエーテル抽出、飽和NaCl水溶液洗浄、Na₂SO₄にて乾燥後、溶媒を留去し、粗(S)-クロマン-2-カルボン酸2.9gを得た。GC 96.2%

【0028】

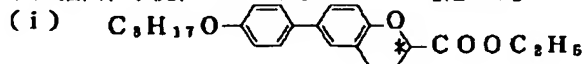
【化51】

(g)



の合成

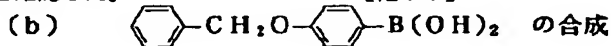
(f)で得た(S)-クロマン-2-カルボン酸2.7g (15mM)のエタノール150ml溶液に、濃H₂SO₄ 2mlを加え、7時間還流攪拌した。反応終了後、溶媒を濃縮し、エーテル抽出、水洗、Na₂SO₄



の合成

N₂気流下、触媒量のPd[PPh₃]₄に(h)で得た(S)-6-プロモクロマン-2-カルボン酸エチルエステル1g (3.5mM)のベンゼン20ml溶液、2M-Na₂SO₃水溶液及び4-オクチルオキシフェニルボロン酸1.07g (3.85mM)のエタノール10ml溶液を加え、4時間還流攪拌した。反応終了後、水に注加し、ベンゼン抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、残留分をヘキサン-ベンゼン(1:1)を溶出液としたシリカゲルカラムクロマトグラフィ、次いでアセトン-エタノール混合溶媒による再結晶にて精製し、(S)-6-(4-オクチルオキシフェニル)-クロマン-2-カルボン酸エチルエステル0.74gを得た。

【0031】このものの純度はHPLCで100%であり、またIR及びMass分析にて410に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。



の合成

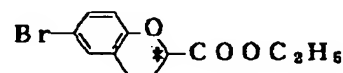
N₂気流下、I₂にて活性化したMg 2.03g (86.3mM)に対し、(a)で得た4-ベンジルオキシプロモベンゼン20g (76mM)のTHF 100ml溶液の約1/5量を加え、加熱した。反応開始後、残り

にて乾燥後、溶媒を留去し、残留分をGTOにて蒸留し、(S)-クロマン-2-カルボン酸エチルエステル2.56gを得た。b.p. 95~100℃/0.2 torr, GC 97.2%, [α]_D = -5.6° (c = 1.0, CHCl₃)

【0029】

【化52】

(h)



の合成

(g)で得た(S)-クロマン-2-カルボン酸エチルエステル2.47g (12mM)を塩化メチレン20mlに溶かし、反応系を0℃に冷却し、Ti(NO₃)₃·3H₂O 0.62g (1.4mM)を加え、さらにBr₂ 0.36mlの塩化メチレン10ml溶液を2時間かけて滴下し、0℃にて1時間攪拌した。反応終了後、希Na₂SO₃水溶液に注加し、塩化メチレン抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、残留分をGTOにて蒸留し、(S)-6-プロモクロマン-2-カルボン酸エチルエステル2.2gを得た。b.p. 115~120℃/0.8 torr, GC 84.7%

【0030】

【化53】

(i)

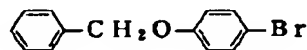
の合成

【0032】このものをメトラ-ホットステージFP-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。

【0033】【実施例2】

【化54】

(a)



の合成

α-クロロトルエン25g (0.19M)、4-プロモフェノール27g (0.15M)、K₂CO₃ 51g (0.37M)及び2-ブタノン300mlから成る混合物を15時間還流攪拌した。反応終了後、析出物を濾別し、濾液をベンゼン抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、残留分をヘキサン-メタノール混合溶媒により再結晶を行い4-ベンジルオキシプロモベンゼン33.9gを得た。GC 98.2%

【0034】

【化55】

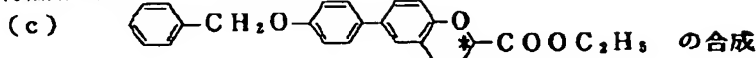
(b)

の合成

のTHF溶液を滴下し、1時間還流攪拌してグリニヤール試薬を調製した。

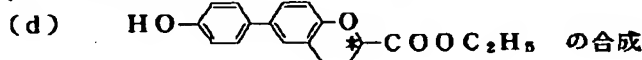
【0035】一方、ホウ酸トリメチル20g (0.15M)のTHF 20ml溶液を0~3℃に冷却し、先に調

製したグリニヤール試薬を滴下し、0℃にて1時間、室温に戻して1時間反応させた。さらに氷冷した10% H_2SO_4 水溶液を滴下し、ベンゼン抽出、水洗、 Na_2SO_4 にて乾燥後、溶媒を留去し、残留分をヘキサン-エーテル混合溶媒にて再結晶を行い、4-ベンジルオキ



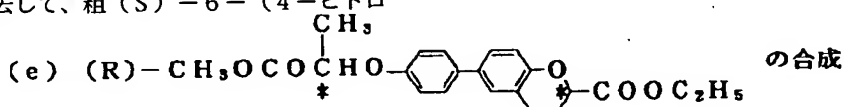
シフェニルボロン酸7.66gを得た。HPLC 91.5%
【0036】
【化56】

実施例1-(i)において、4-オクチルオキシフェニルボロン酸1.07gに替えて(b)で得た4-ベンジ
ルオキシフェニルボロン酸0.88gを用い、他は同様
に操作して、(S)-6-(4-ベンジルオキシフェニ



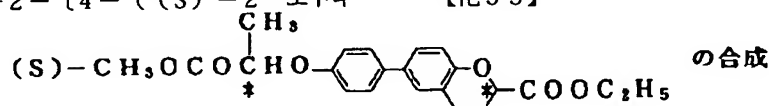
ル)クロマン-2-カルボン酸エチルエステル0.63gを得た。HPLC 93.0%、Mass M^+ 298
【0037】
【化57】

オートクレープに触媒量の10% Pd/C、(c)で得た(S)-6-(4-ベンジルオキシフェニル)クロマン-2-カルボン酸エチルエステル0.63g(1.6mM)及び酢酸エチル20mlを仕込み、水素圧30atmにて4日間室温撹拌した。反応終了後、Pd/Cを



キシフェニル)クロマン-2-カルボン酸エチルエステル0.43gを得た。HPLC 99.4%、Mass M^+ 298
【0038】
【化58】

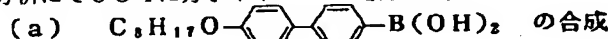
(d)で得た(S)-6-(4-ヒドロキシフェニル)クロマン-2-カルボン酸エチルエステル0.2g(0.6mM)、トリフェニルフォスフィン0.36g(1.3mM)、(S)-乳酸メチル0.21g(2.0mM)及びTHF20mlから成る溶液に、氷冷撹拌下、アゾジカルボン酸エチル0.33g(1.9mM)を滴下し、さらに室温にて7日間反応させた。反応終了後、溶媒を留去し、残留分をベンゼンを溶出液としたシリカゲルクロマトグラフィー、次いで塩化メチレンを展開液とした分取薄層クロマトグラフィー(20×20)にて精製し、(R)-2-[4-(S)-2-エトキシ



シカルボニルクロマン-6-イル)フェノキシ]プロピオン酸メチルエステル95mgを得た。
【0039】このものの純度はHPLCで98.4%であり、またIR及びMass分析にて384に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。
【0040】このものをメトラ-ホットステージFP-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。
【0041】【実施例3】
【化59】

実施例2-(e)において(S)-乳酸メチル0.21gに替えて、(R)-乳酸メチルを用い、他は同様に操作して、(S)-2-[4-(S)-2-エトキシカルボニルクロマン-6-イル)フェノキシ]プロピオン酸メチルエステル102mgを得た。

【0042】このものの純度はHPLCで99.0%であり、またIR及びMass分析にて384に分子イ



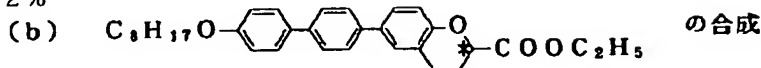
ンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。
【0043】このものをメトラ-ホットステージFP-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。
【0044】【実施例4】
【化60】

実施例2-(b)において4-ベンジルオキシプロモベ 50 ンゼン20gに替えて、4-オクチルオキシ-4'-ブ

ロモビフェニル27.4gを用い、他は同様に操作して、4-ビフェニル-4'-ボロン酸10.8gを得た。HPLC 84.2%

【0045】

【化61】



実施例1-(i)において4-オクチルオキシフェニルボロン酸1.07gに替えて(a)で得た4-オクチルオキシビフェニル-4'-ボロン酸1.25gを用い、他は同様に操作して、(S)-6-(4-オクチルオキシビフェニル-4'-イル)クロマン-2-カルボン酸エチルエステル0.53gを得た。

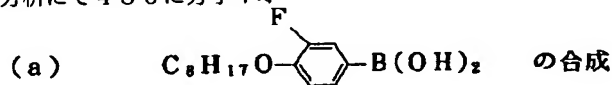
ンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

【0047】このものをメトラ-ホットステージFP-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。

【0048】【実施例5】

【化62】

【0046】このものの純度はHPLCで98.7%であり、またIR及びMass分析にて486に分子イオ

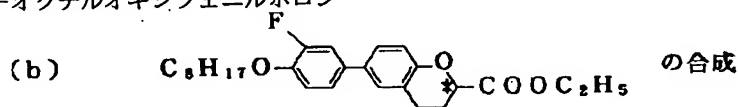


実施例2-(b)において、4-ベンジルオキシプロモベンゼン20gに替えて、3-フルオロ-4-オクチルオキシプロモベンゼン23gを用い、他は同様に操作して、3-フルオロ-4-オクチルオキシフェニルボロン

酸7.2gを得た。

【0049】

【化63】



実施例1-(i)において、4-オクチルオキシフェニルボロン酸1.07gに替えて(a)で得た3-フルオロ-4-オクチルオキシボロン酸1.14gを用い、他は同様に操作して、(S)-6-(3-フルオロ-4-オクチルオキシフェニル)クロマン-2-カルボン酸エチルエステル0.55gを得た。

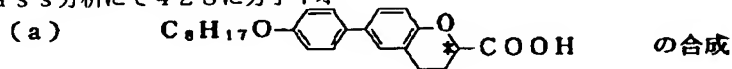
ンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

【0051】このものをメトラ-ホットステージFP-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。

【0052】【実施例6】

【化64】

【0050】このものの純度はHPLCで99.8%であり、またIR及びMass分析にて428に分子イオ

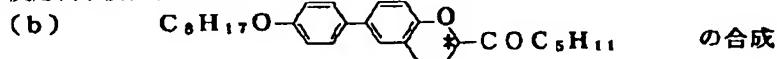


実施例1-(i)で得られる(S)-6-(4-オクチルオキシフェニル)クロマン-2-カルボン酸エチルエステル0.3g(0.7mM)をメタノール25ml、THF 10ml及び水3mlから成る混合液に溶かし、95%NaOH0.21g(5.2mM)を加え、1時間還流撹拌した。反応終了後、水に注加し、濃HC

lにて酸性とし、ベンゼン抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、粗(S)-6-(4-オクチルオキシフェニル)クロマン-2-カルボン酸0.24gを得た。Mass M+382

【0053】

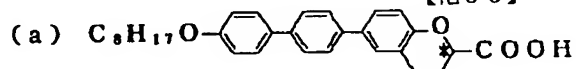
【化65】



N₂気流下、Mg 0.16g(6.6mM)にn-ペンチルブロマイド1g(6.6mM)のエーテル20ml溶液の約1/3量を加え、加熱した。反応開始後、残りのエーテル溶液を滴下し、さらに1時間還流撹拌してグリニヤール試薬を調製した。

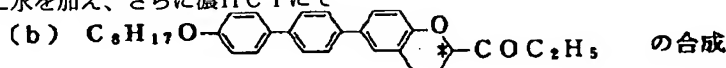
【0054】一方、N₂気流下、(a)で得た(S)-6-(4-オクチルオキシフェニル)クロマン-2-カルボン酸0.24g(0.65mM)をTHF20mlにて加熱溶解し、放冷後、ビス(1,3-ジフェニルホスフィン)プロパン)ニッケル(II)クロライドを触媒

量加え15分間攪拌した。次いで先に調製したグリニヤール試薬を滴下し、12時間室温攪拌した。反応終了後、希HCl水溶液に注加し、ベンゼン抽出、水洗、 Na_2SO_4 にて乾燥後、溶媒を留去し、残留分をヘキサン-ベンゼン(1:1)を溶出液としたシリカゲルカラムクロマトグラフィー、次いでメタノール-アセトン混合溶媒からの再結晶にて精製し、(S)-6-(4-オクチルオキシフェニル)-2-ヘキサノイルクロマン0.17gを得た。



の合成

実施例4-(b)で得られる(S)-6-(4-オクチルオキシビフェニル-4'-イル)クロマン-2-カルボン酸エチルエステル0.25g(0.51mM)をメタノール25ml、THF20ml及び水3mlから成る混合液に懸濁させ、95%NaOH 0.2g(4.9mM)を加え、30分間加熱攪拌した。反応終了後、溶媒を留去し、残留分に水を加え、さらに濃HClにて



の合成

N_2 気流下、Mg 0.22g(9.14mM)に、n-エチルプロマイド1g(9.17mM)のエーテル20ml溶液の約1/3量を加え、加熱した。反応開始後、残りのエーテル溶液を滴下し、さらに2時間還流攪拌してグリニヤール試薬を調製した。

【0059】一方、 N_2 気流下、(a)で得た(S)-6-(4-オクチルオキシビフェニル-4'-イル)クロマン-2-カルボン酸0.24g(0.65mM)をTHF20mlにて加熱溶解し、放冷後、ビス(1,3-ジフェニルホスフィン)プロパン)ニッケル(II)クロライドを触媒量加え10分間攪拌した。次いで先に調製したグリニヤール試薬を滴下し、30時間室温攪拌した。反応終了後、希HCl水溶液に注加し、エーテル抽出、氷冷水にて洗浄、 Na_2SO_4 にて乾燥後、溶媒を留去し、残留分をベンゼンを溶出液としたシリカゲルカラムクロマトグラフィー及び分取薄層クロマトグラフィー(20×20)、次いでアセトンからの再結晶にて精製し、(S)-6-(4-オクチルオキシビフェニル-4'-イル)-2-プロパノイルクロマン73mgを得た。

【0060】このものの純度はHPLCで99.8%であり、またIR及びMass分析にて470に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

【0061】このものをメトラ-ホットステージFPR-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。

【0062】【実施例8】

【0055】このものの純度はHPLCで99.1%であり、またIR及びMass分析にて436に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

【0056】このものをメトラ-ホットステージFPR-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。

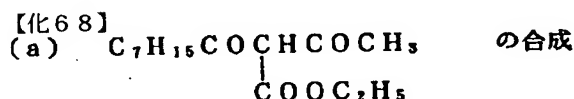
【0057】【実施例7】

【化66】

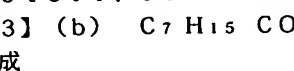
酸性とし、析出物を濾取、水洗し、乾燥した後、粗(S)-6-(4-オクチルオキシビフェニル-4'-イル)クロマン-2-カルボン酸0.25gを得た。Mass M+458

【0058】

【化67】

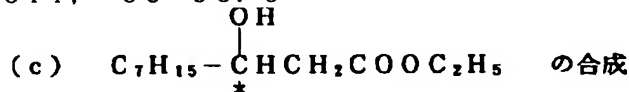


Mg 37.5g(1.54M)にエタノール34ml及び四塩化炭素7mlを加え、室温に放置すると数分後に反応が開始し、還流が始まった。ここにベンゼン140mlを系の温度が60~70℃になるように調製しながら滴下し、次いでアセト酢酸エステル200g(1.54M)、エタノール140ml及びベンゼン140mlから成る混合液を系の温度が80℃以下になるように滴下した。滴下終了後Mgが完全に溶けるまで還流した。反応混合物を室温まで放冷した後、湯浴上にて30~35℃に反応温度を保ち、n-オクタノイルクロライド227g(1.4M)のベンゼン210ml溶液を1時間を要して徐々に滴下し、さらに同温度にて2時間反応させた。反応終了後、氷冷水700mlで希釈し、30%H₂SO₄水溶液にて酸性とし、ベンゼン層を分取し、水洗、 Na_2SO_4 にて乾燥後、溶媒を留去し、残留分を減圧蒸留し、エチルn-オクタノイルアセトアセテート253gを得た。bp. 120~123℃/0.9~1.5 torr, GC 98.6%

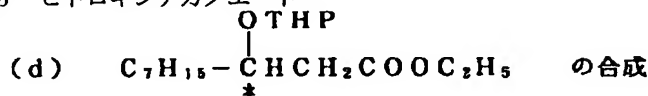
【0063】(b) $\text{C}_{27}\text{H}_{44}\text{O}_4$  H_5 の合成

エタノール140mlにNa 5g(0.21M)を溶かし、(a)で得たエチルn-オクタノイルアセトアセテート250g(0.98M)を加え、湯浴上にて4時間煮沸した。放冷後、氷冷水に注加し、30%H₂SO₄

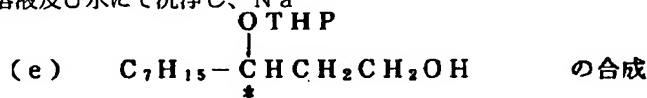
水溶液にて酸性とし、ベンゼン抽出、水洗、 Na_2SO_4 にて乾燥後、溶媒を留去し、残留分を減圧蒸留し、エチル n -オクタノイルアセテート160gを得た。b.p. 89~99℃/0.3 torr, GC 95.6%
【0064】
【化69】



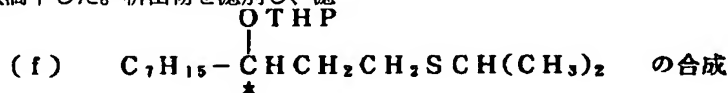
オートクレープに Ru_2Cl_4 [(+)-BINAP] 105gを得た。b.p. 89~108℃/0.3~0.4 torr, GC 99%, o.p. 99% ee, $[\alpha]_D^{19} = -5.37^\circ$ (neat)
【0065】
【化70】



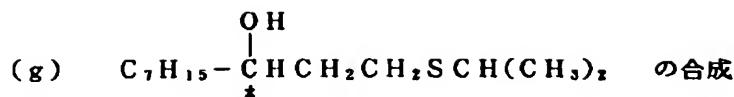
(c) で得たエチル β -ヒドロキシデカノエート18g (83mM)、3,4-ジヒドロ-2H-ピラン10.5g (0.12M) 及び塩化メチレン180mlから成る溶液に、ピリジニウム p -トルエンスルホン酸1.0g (4.1mM) を加え、16時間室温撹拌した。反応終了後、5% NaHCO_3 溶液及び水にて洗浄し、 Na_2SO_4 乾燥後、溶媒を留去し、光学活性な粗エチル β -テトラヒドロピラニルオキシデカノエート33.5gを得た。GC 94.5%
【0066】
【化71】



氷冷撹拌下、 LiAlH_4 4.6g (0.12M) とエーテル100mlから成る懸濁液に(d)で得た粗エチル β -テトラヒドロピラニルオキシデカノエート33g (0.11M) を滴下し、さらに反応系を室温まで徐々に上げ、5時間撹拌した。反応終了後、系を-5℃まで冷却し、酢酸エチル24ml、クロロホルム160ml及び水24mlを順次滴下した。析出物を濾別し、濾液を飽和 NaCl 水溶液にて洗浄、 Na_2SO_4 にて乾燥後、溶媒を留去し、光学活性な3-テトラヒドロピラニルオキシデカノール23.3gを得た。GC 96.1%
【0067】
【化72】



(e) で得た粗3-テトラヒドロピラニルオキシデカノール23g (0.09M) のピリジン100ml溶液を、0℃以下に冷却し、 p -トルエンスルホン酸クロライド25.8g (0.13M) を加え、同温度にて5時間撹拌した。反応混合物を水に注加し、エーテル抽出、水にて洗浄、 Na_2SO_4 にて乾燥後、溶媒を留去し、粗トシレート体28.7gを得た。
【0068】一方、メタノール150mlにナトリウム10g (0.43M) を溶かし、イソプロピルメルカプタン22ml (0.28M) を加え、室温にて2時間撹拌した。さらに先に調製したトシレート体のメタノール50ml溶液を滴下し、50℃にて16時間反応させた反応混合物を水に注加し、エーテル抽出、水洗を行い、 Na_2SO_4 にて乾燥後、溶媒を留去し、光学活性な粗1-イソプロピルチオ-3-テトラヒドロピラニルオキシデカン19.7gを得た。GC 78.5%
【0069】
【化73】

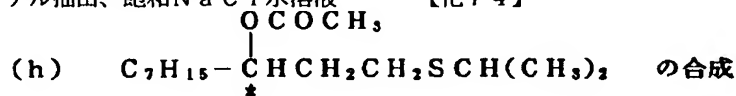


(f) で得た粗 1-イソプロピルチオ-3-テトラヒドロピラニルオキシデカン 10 g (0.04 M)、酢酸 40 ml、THF 30 ml 及び水 20 ml から成る溶液を加え、55~60℃にて28時間加熱撹拌した。反応混合物を水に注加し、エーテル抽出、飽和 NaCl 水溶液

にて洗浄し、 Na_2SO_4 にて乾燥後、溶媒を留去し、光学活性な粗 1-イソプロピルチオデカノール-3 を得た。GC 56%

【0070】

【化74】

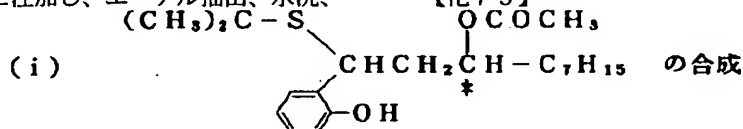


(g) で得た粗 1-イソプロピルチオデカノール-3 10 g (0.04 M)、無水酢酸 40 ml、ピリジン 40 ml 及び N, N-ジメチル-4-アミノピリジン 1.1 g (9 mM) から成る混合物を室温にて24時間撹拌した。反応混合物にメタノール 60 ml を徐々に加え、さらに氷冷水 100 ml に注加し、エーテル抽出、水洗、

Na_2SO_4 にて乾燥後、溶媒を留去し、残留分を GTO にて蒸留し、光学活性な粗 3-アセトキシ-1-イソプロピルチオデカン 7.7 g を得た。bp. 110~115℃/0.25 torr, GC 89.6%

【0071】

【化75】

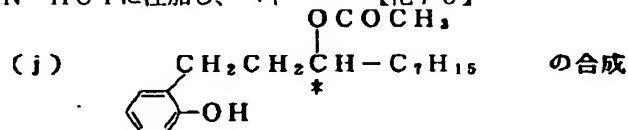


フェノール 9.4 g (0.1 M) の塩化メチレン 70 ml 溶液に (g) で得た粗 3-アセトキシ-イソプロピルチオデカン 8.9 g (0.03 M) を加え、反応系をアルゴン置換し、-60℃まで冷却した。さらに、塩化スルフルリル 3.1 ml (0.04 M) をシリンジにて滴下し、同温度にて15分間反応させた後、トリエチルアミン 23 ml (0.17 M) の塩化メチレン 24 ml 溶液を反応系の温度が-40℃以下に保つように滴下した。【0072】反応終了後、1N-HCl に注加し、ヘキ

サン抽出、飽和 NaHCO_3 水溶液及び水にて洗浄を行い、 Na_2SO_4 にて乾燥し、溶媒を留去後、残留分をヘキサン-酢酸エチル (30:1) を溶出液としたシリカゲルカラムクロマトグラフィーにて精製し、光学活性な粗 2-(3'-アセトキシ-1'-イソプロピルチオデシル) フェノール 3.05 g を得た。GC 72.1%, Mass M^+ 466

【0073】

【化76】

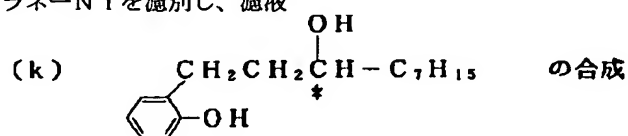


ラネー N1 約 24 cm³ を 25 ml のエタノールにとり、(i) で得た粗 2-(3'-アセトキシ-1'-イソプロピルチオデシル) フェノール 3 g (8.1 mM) のエタノール 25 ml 溶液を加え、19時間還流撹拌した。反応終了後、熱濾過にてラネー N1 を濾別し、濾液

を濃縮し、光学活性な粗 2-(3'-アセトキシデシル) フェノール 2.37 g を得た。GC 51%

【0074】

【化77】



氷冷撹拌下、LiAlH₄ 3.0 g (0.08 M) とエーテル 70 ml から成る懸濁液に (j) で得た粗 2-

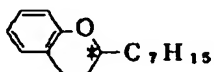
(3'-アセトキシデシル) フェノール 2.3 g (0.01 M) のエーテル 30 ml 溶液を滴下し、さらに反応

系を室温まで徐々に上げた。反応終了後、氷冷した希HCl水溶液に注加し、エーテル抽出、飽和NaCl水溶液にて洗浄し、Na₂SO₄にて乾燥後、溶媒を留去し、光学活性な粗2-(3'-ヒドロキシデシル)フェノール1.87gを得た。GC 51.3%

【0075】

【化78】

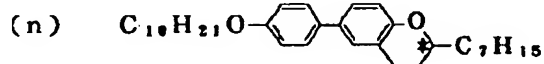
(1)



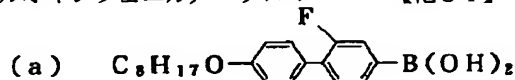
の合成

(k)で得た粗2-(3'-ヒドロキシデシル)フェノール1.87g (7.5mM)とベンゼン50mlから成る懸濁液にp-トルエンスルホン酸一水和物0.81g (4.3mM)を加え、8時間還流撹拌した。反応終了後、飽和NaHCO₃水溶液に注加し、有機層を水洗、Na₂SO₄にて乾燥後、溶媒を留去し、光学活性な粗2-ヘプチルクロマン1.59gを得た。GC 58.5%

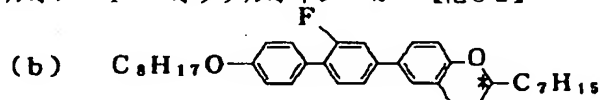
【0076】



N₂気流下、触媒量のPd[PPh₃]₄に(m)で得た2-ヘプチル-6-ブロモクロマン0.5g (1.6mM)のベンゼン10ml溶液、2M-NaCO₃水溶液2ml、4-デシルオキシフェニル硼酸0.49g (1.7mM)のエタノール5ml溶液を加え、6時間還流撹拌した。反応終了後、水に注加し、ベンゼン抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、残留分をヘキサン-ベンゼン(10:1)を溶出液としたシリカゲルカラムクロマトグラフィー、次いでアセトン-メタノール混合溶媒からの精製にて光学活性な2-ヘプチル-6-(4-デシルオキシフェニル)-クロマ



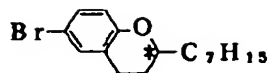
実施例2-(b)において4-ベンジルオキシブロモベンゼン20gに替えて、2-フルオロ-4'-オクチルオキシ-4-ブロモビフェニル28.8gを用い、他は同様に操作して、2-フルオロ-4'-オクチルオキシ



実施例8-(n)において4-デシルオキシフェニル硼酸0.49gに替えて(a)で得たフルオロ-4'-オクチルオキシビフェニル-4-硼酸0.6gを用い、他は同様に操作して、光学活性な2-ヘプチル-6-(2'-フルオロ-4-オクチルオキシビフェニル-4-イル)-クロマン0.15gを得た。

【化79】

(m)



の合成

(1)で得た粗2-ヘプチルクロマン1.59g (5.1mM)の塩化メチレン30ml溶液を0℃に冷却し、Tl(NO₃)₃·3H₂O 0.27g (0.6mM)を加え、さらにBr₂ 0.21mlの塩化メチレン10ml溶液を30~40分間要して滴下した。

【0077】反応終了後、希Na₂SO₃水溶液に注加し、析出物を濾別し、濾液を塩化メチレンにて抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、残留分をGTOにて蒸留し、光学活性な粗2-ヘプチル-6-ブロモクロマン0.78gを得た。bp. 160℃/0.7torr, GC 71.8%, Mass M⁺ 310, 312

【0078】

【化80】

ン0.27gを得た。[α]_D²⁷ = -53.6° (c = 1, CHCl₃)

【0079】このものの純度はHPLCで97.7%であり、またIR及びMass分析にて465に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

【0080】このものをメトラ-ホットステージFP-82付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表1に示す。

【0081】〔実施例9〕

【化81】

ビフェニル-4-硼酸9.9gを得た。HPLC 87.3%

【0082】

【化82】

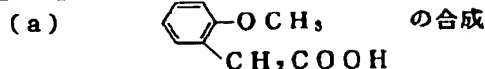
【0083】このものの純度はHPLCで97.2%であり、またIR及びMass分析にて530に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

【0084】このものをメトラ-ホットステージFP-82付き偏光顕微鏡下で相転移温度を観察した。その結

果を後掲表1に示す。

【0085】〔実施例10〕

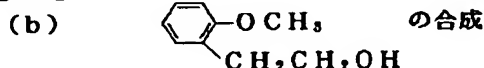
【化83】



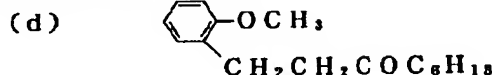
o-メトキシフェニルアセトニトリル299g (2.03M) をメタノール500mlに溶かし、85% KOH 170gの水200ml水溶液を加え、NH₃ 臭が無くなるまで2日間還流撹拌した。反応混合物を氷冷水に注加し、析出物を濾取し、氷冷水にて洗淨し、さらに減圧乾燥して、o-メトキシフェニル酢酸319gを得た。Mass M⁺ 166

【0086】

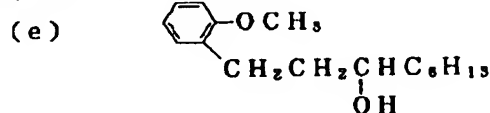
【化84】



氷冷撹拌下、LiAlH₄ 15.6g (0.41M) と THF 200ml から成る懸濁液に、(a) で得た o-メトキシフェニル酢酸50g (0.3g) の THF 200ml 溶液を滴下し、さらに反応系を室温まで徐々に上



N₂ 気流下、Mg 4.6g (18.9mM) にエーテル 40ml を加え、さらに (c) で得た 2-(o-メトキシフェニル) エチルプロマイド 31.2g (0.14M) のエーテル 80ml 溶液の約 1/3 量を加え加熱し、反応開始後、残りのエーテル溶液を滴下し 90 分間還流撹拌した。反応系を 0℃ に冷却し、CdCl₂ 3.3g (7.3mM) を少量ずつ加えた後、45 分間還流撹拌した。反応混合物からエーテルを留去し、ベンゼン 90ml を加え、再度留去し、ベンゼン 100ml を加え溶媒置換した。室温まで放冷した後、ヘプタノイルクロライド 19g (0.12M) のベンゼン 10ml 溶



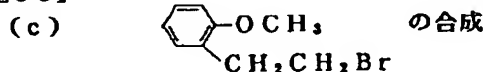
(d) で得た 2-(2-ヘプタノイルエチル) アニソール 19.4g (78.2mM) のエタノール 150ml 溶液に、NaBH₄ 3.5g (93mM) を少量ずつ加え、4 時間室温撹拌した。反応系からエタノールを留去し、残留分に水 100ml を加え、エーテル抽出、飽和 NaCl 水溶液にて洗淨、Na₂SO₄ にて乾燥後、溶媒を留去し、粗 2-(3'-ヒドロキシノニル) アニソール 20.7g を得た。GC 84.2%

【0090】

げ、8 時間撹拌した。反応混合物を氷冷水に注加し、濃 HCl にて酸性とし、エーテル抽出、飽和 NaCl 水溶液にて洗淨、Na₂SO₄ にて乾燥後、粗 2-(o-メトキシフェニル) エタノール 46g を得た。GC 99%

【0087】

【化85】



(b) で得た 2-(o-メトキシフェニル) エタノール 20g (0.13M) の四塩化炭素 60ml 溶液に、0℃ にて三臭化リン 19g (0.06M) を滴下し、さらに 0℃ で 1 時間、室温に戻して 3 時間撹拌した。反応混合物を氷冷水に注加し、四塩化炭素にて抽出、水洗、Na₂SO₄ にて乾燥後、溶媒を留去し、残留分を減圧蒸留し、2-(o-メトキシフェニル) エチルプロマイド 14.2g を得た。bp. 62~68℃/0.3 torr, GC 96.6%

【0088】

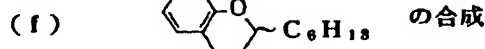
【化86】

液を滴下し、40 分間還流撹拌した。反応混合物を氷冷水に注加し、希 H₂SO₄ 水溶液 80ml を加え、有機層を分取し、溶媒留去後、さらに 10%-NaOH-水-エタノール溶液 50ml を加え、水にて希釈し、ベンゼン抽出、水洗、Na₂SO₄ にて乾燥、溶媒を留去し、残留分を GTO にて蒸留し、2-(2-ヘプタノイルエチル) アニソール 19.5g を得た。bp. 135~140℃/1.0 torr, GC 78.3%

【0089】

【化87】

【化88】

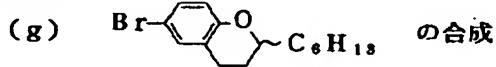


(e) で得た粗 2-(3'-ヒドロキシノニル) アニソール 20g (91.7mM)、酢酸 100ml 及び 48% HBr 150ml から成る混合物を 60 時間還流撹拌した。反応混合物を氷冷水に注加し、エーテル抽出、水洗、希 NaOH 水溶液にて洗淨、水洗を順次行い、N

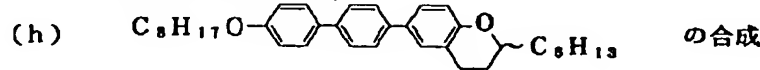
Na₂SO₄にて乾燥後、溶媒を留去し、残留分をヘキサンを溶出液としたシリカゲルカラムクロマトグラフィー、次いでGTOにて蒸留し、粗2-ヘキシルクロマン 3.8gを得た。b.p. 95℃/0.6 torr, GC 79.3%

【0091】

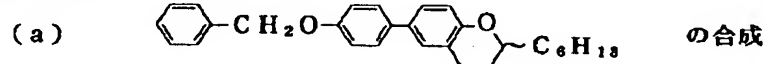
【化89】



(f) で得た粗2-ヘキシルクロマン 3.6g (16.4 mM) の塩化メチレン 30 ml 溶液を0℃に冷却し、

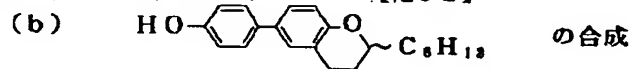


N₂ 気流下、触媒量の Pd (p p h₃)₄ に (g) で得た 2-ヘキシル-6-ブロモクロマン 1g (3.3 mM) のベンゼン 40 ml 溶液、2M-Na₂CO₃ 水溶液 5 ml 及び実施例 4-(a) で得た 4-オクチルオキシビフェニルボロン酸 1.2g (3.7 mM) のエタノール 30 ml 溶液を加え、6時間還流撹拌した。反応終了後、水に注加し、ベンゼン抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、残留分をヘキサン-塩化メチレン (5:1) を溶出液としたシリカゲルカラムクロマトグラフィー、次いでアセトンから再結晶を行い 2-ヘキシル-6-(4-オクチルオキシビフェニル-4'-

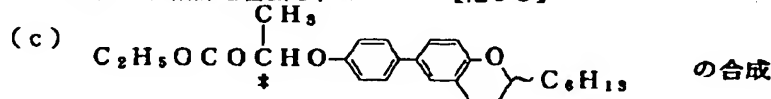


実施例 10-(h) において 4-オクチルオキシビフェニル-4'-ボロン酸 1.2g に替えて実施例 2-

(b) で得た 4-ベンジルオキシフェニルボロン酸 0.84g を用い他は同様に操作して、2-ヘキシル-6-



オートクレープに触媒量の 10% Pd/C、(a) で得た 2-ヘキシル-6-(4-ベンジルオキシフェニル)クロマン 0.53g (1.3 mM) 及び酢酸エチル 25 ml を仕込み、水素圧 3.5 atm にて 4 日間室温撹拌した。反応終了後、Pd-C を濾別し、溶媒を留去し、2



(b) で得た 2-ヘキシル-6-(4-ヒドロキシフェニル)クロマン 0.2g (0.6 mM)、トリフェニルレオスフィン 0.36g (1.3 mM)、(S)-乳酸エチル 0.21g (2.0 mM) 及び THF 20 ml から成る溶液に、氷冷撹拌下、アゾジカルボン酸エチ

ル 0.84g (1.9 mM) を加えさらに Br₂ 1.3g (8.2 mM) の塩化メチレン 10 ml 溶液を 30~40 分間要して滴下した。反応終了後、希 Na₂SO₃ 水溶液に注加し、析出物を濾別し、濾液を塩化メチレンにて抽出、水洗、Na₂SO₄にて乾燥後、溶媒を留去し、残留分を GTO にて蒸留し、2-ヘキシル-6-ブロモクロマン 2.7g を得た。b.p. 135℃/0.7 torr, GC 68.1%

【0092】

【化90】

イル)クロマン 0.44g を得た。

【0093】このものの純度は HPLC で 98.8% であり、また IR 及び Mass 分析にて 498 に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

【0094】このものをメトラ-ホットステージ FP-82 付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表 5 に示す。

【0095】【実施例 11】

【化91】

(4-ベンジルオキシフェニル)クロマン 0.53g を得た。HPLC 98.8%, Mass M⁺ 400

【0096】

【化92】

2-ヘキシル-6-(4-ヒドロキシフェニル)クロマン 0.33g を得た。HPLC 99.7%, Mass M⁺ 310

【0097】

【化93】

0.33g (1.9 mM) を滴下し、さらに室温にて 7 日間反応させた。反応終了後、溶媒を留去し、残留分をベンゼン-ヘキサン (1:1) を溶出液としたシリカゲルカラムクロマトグラフィー、次いでメタノールからの再結晶にて精製し、(R)-2-[4-(2-ヘキシ

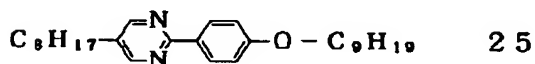
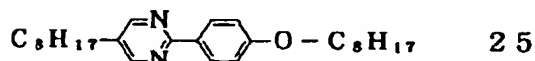
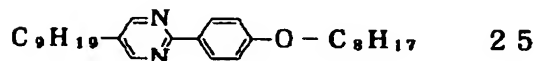
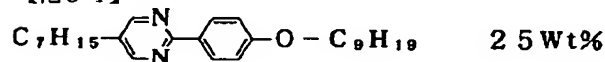
ルクロマン-6-イル) フェノキシ) プロピオン酸エチルエステル 99mg を得た。

【0098】このものの純度は HPLC で 99.1% であり、また IR 及び Mass 分析にて 410 に分子イオンピークが認められたこと、並びに用いた原料より、得られた物質が目的物であることを確認した。

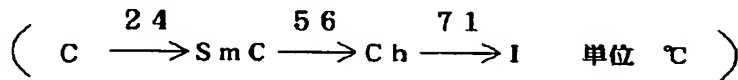
【0099】このものをメトラ-ホットステージ FP-82 付き偏光顕微鏡下で相転移温度を観察した。その結果を後掲表 4 に示す。

【0100】〔実施例 12〕

〔化 94〕

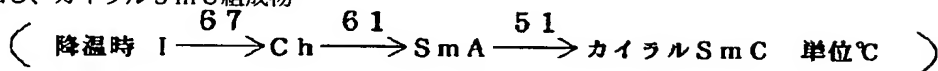


上記 4 種のピリミジン化合物から成る母体液晶
【外 1】



を調製した。この母体液晶に実施例 1 で得られた化合物を 5Wt% 添加し、カイラル SmC 組成物

【外 2】



を調製した。

【0101】この組成物をポリイミド塗布し、ラビング処理を施した透明電極付きガラス基板から作成した 2μm ギャップの液晶セルに注入して液晶素子を作成した。

【0102】この液晶素子を 2 枚の偏光板に挟み、±5V/μm、200Hz の矩形波を印加して、透過光強度の変化から応答時間を求めた。又、ソーヤー・タワー法にて自発分極を測定し、印加電圧の極性反転時の消光位の移動角度よりチルト角度を測定した。その結果を下表 1 に示す。

【0103】

【表 1】

表 1

測定温度 (°C)	45	37	32	25
応答時間 (μsec)	172	223	268	328
自発分極 (nC/cm ²)	-2.8	-2.8	-3.7	-3.7
チルト角度 (°)	16.9	21.2	22.5	24.7



【0104】〔実施例 13〕実施例 12 において、実施例 1 で得られた化合物に替えて、実施例 6 で得られた化合物を同様の母体液晶に 5Wt% 添加して作成したカイラル SmC 液晶組成物を用いて実施例 12 と同様に応答時間、自発分極並びにチルト角度を測定した結果を下記に示す。なお、作成したカイラル SmC 液晶組成物の降温時の相転移温度 (°C) は

【外 3】

であった。

【0105】

【表2】

表 2

測定温度 (°C)	43	36	31	25
応答時間(μsec)	173	221	284	482
自発分極(nC/cm ²)	-0.4	-0.9	-1.5	-1.5
チルト角度 (°)	7.2	10.2	12.4	14.1

10

【0106】〔実施例14〕実施例12において、実施例1で得られた化合物に替えて、実施例11で得られた化合物を同様の母体液晶に5Wt%添加して作成したカイラルSmC液晶組成物を用いて実施例12と同様に応

答時間、自発分極並びにチルト角度を測定した結果を下記に示す。なお、作成したカイラルSmC液晶組成物の降温時の相転移温度(°C)は

【外4】

41

I $\xrightarrow{65}$ Ch $\xrightarrow{56}$ SmA $\xrightarrow{41}$ カイラルSmC

であった。

【0107】

【表3】

表 3

測定温度 (°C)	41	34	29	25
応答時間(μsec)	42	161	220	268
自発分極(nC/cm ²)	+1.3	+2.6	+2.6	+3.9
チルト角度 (°)	7.1	14.6	17.5	18.9

【0108】

【表4】

表 4

実施例 番号	相転移温度 (°C)					
	C	SmX	カイラル SmC	SmA	Cho	Iso
1	• 76.8					•
2	• 87.8					•
3	• 63.7					•
4	• 146.5		• 158.2	• 189.7		•
5	• 58.3					•
6	• 80.4			(• 74.0)		•
7	• 130.5		• 152.2	• 228.4		•
8	• 67.2			• 93.4		•
9	• 71.9		• 123.5	• 159.6	• 173.2	•
11	• 38.1					•

【0109】

【表5】

表 5

実施例 番 号	相転移温度 (°C)				
	C	SmX	SmC	SmA	Cho Iso
10	・ 150.5		・ 183.6	・ 212.1	・

フロントページの続き

(51)Int.Cl.⁵

G 0 9 F 9/35

識別記号

3 0 3

庁内整理番号

7926-5G

F I

技術表示箇所

(72)発明者 藤井 恒宣

埼玉県草加市稻荷 1-7-1 関東化学株
式会社中央研究所内

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.